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1. Schlesinger, E. B.: Am. J. Med. 1:518 (Nov.) 1946.

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LIGATION OF THE INFERIOR VENA CAVA IN THROMBOEMBOLISM

Report of 36 Cases

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MUCH has appeared in the medical literature during the past several years on venous thrombosis and pulmonary embolism. The high incidence of thrombosis in the deep veins of the lower extremities and the dangers attending such a process have been stressed. It is the purpose of this presentation to re-emphasize the importance of this disease, to discuss its surgical management once pulmonary infarction has occurred, and to report on 36 patients whom we have treated by ligation of the inferior vena cava within the past 3 years. To date no authors have advocated *routine* ligation of the inferior vena cava in cases of pulmonary embolism from venous thrombosis of the deep veins of the lower limbs, or from a clinically hidden source. It is our belief that this procedure will offer the patient with pulmonary embolism the best prognosis for both immediate and ultimate results.

IMPORTANCE AND SIGNIFICANCE OF THROMBOEMBOLISM

Despite the abundance of material in the literature on the subject of venous thrombosis and pulmonary embolism, the importance of the disease is as yet not fully appreciated.

Welch and Faxon in a group of 250 cases at the Massachusetts General Hospital found that the ratio of fatal embolism to recognizable phlebitis, without regard to the type or duration of the disease, was 1 to 25 (4 per cent). If these figures were adjusted to show the incidence of fatal embolism in cases of recognizable phlebothrombosis alone, the ratio undoubtedly would be much higher. Welch and Faxon found, moreover, that 1 patient out of 3 (33⅓ per cent) with phlebitis suffered pulmonary infarction at some stage of the disease.

Barker and others (2), in a statistical study of 1,665 cases of postoperative venous thrombosis and pulmonary embolism at the Mayo Clinic, have concluded that if nonfatal embolism has occurred, the chance that a fatal embolism will follow is slightly less than 1 in 5 (20 per cent), and that the chances of subsequent embolism, fatal or nonfatal, are about 3 in 10 (30 per cent). They state that if all fatal embolisms preceded by clinically diagnosed sublethal emboli could be prevented, the total number of fatal embolisms would be reduced more than one-third.

McCartney, in a study of 25,771 autopsy records, found 4,070 deaths which he considered to be postoperative mortalities. Among this group thromboembolism was present in 471 instances (11.5 per cent), and death was believed to have been caused by pulmonary embolism in 216 (5.3 per cent).

Death from pulmonary embolism may be due to a large clot which occludes the main

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pulmonary artery or its left and right branches; it may also result from asphyxia when large areas of the lungs are infarcted, from failure of the right side of the heart in the face of rapidly rising pulmonary arterial pressures proximal to the embolic occlusions, or from peripheral circulatory failure due to an insufficient venous return to the left atrium. Perhaps equally as important are the deaths which result from very small emboli as a result of various autonomic reflexes. DeTakats and Fowler state that they have shown that patients may die from a small embolus which occludes a vessel to an insignificant area of the lung. On the basis of animal experiments they believe that a widespread radiation of autonomic reflexes, predominently vagal, occurs during embolism. These produce bronchoconstriction, increased bronchial secretion, inhibition of the heart, depression of blood pressure and other effects through smooth muscle spasm, including intestinal colic.

Pulmonary embolism which does not produce death may result in serious lung complications, including necrosis, cavitation, abscess and fibrosis.

Pathological demonstrations have shown that a very high percentage of all pulmonary infarctions, even in patients with heart disease, result from emboli which have their origin in the deep veins of the lower extremities. Allen, Linton, and Donaldson state that Castleman found this to be true in approximately 95 per cent of cases studied at autopsy.

In the female a rather frequent source of pulmonary emboli is thrombosis in the pelvic veins complicating postpartum or postabortal sepsis or operative procedures upon the pelvic viscera. These thrombi may be bland or septic. In the case of bland thrombosis, propagation into the hypogastric vein with breaking off of a portion of the clot will produce pulmonary infarction. In this instance ligation of the inferior vena cava will completely protect against further pulmonary emboli from this source, since it is thought that the ovarian veins will not yield emboli of significant size in bland thrombosis (17). If the thrombi are infected or septic, fragmentation of the clot with discharge of septic emboli may produce not only pulmonary infarction, but pyemia. In this case ligation of the inferior vena cava alone may not suffice, since small, bacteria-laden emboli may continue to enter the general circulation through the ovarian veins. Simultaneous ligation of these veins is therefore to be recommended.

Nelson, Jones, and Collins found a mortality rate of 100 per cent in 30 cases of pelvic thrombophlebitis not operated upon, but state that, in general, the literature accredits the disease with a 50 per cent mortality. These authors had ligated the inferior vena cava in 8 cases at the time their paper was published. The ovarian veins were interrupted simultaneously in 3 cases. One death occurred following operation in a moribund patient who was offered her only chance of recovery through surgery. The mortality rate was 12.5 per cent in the cases operated upon, or one-eighth as high as in those not operated upon.

Thus in cases of pulmonary infarction with no apparent source for emboli, ligation of the inferior vena cava will protect from two very important sources, namely, the veins of the lower extremities and the pelvic veins, except the ovarians.

VARIOUS METHODS OF TREATMENT

We have been discouraged by the results of heparin and dicoumarol therapy in patients in whom pulmonary embolism has occurred. This is true in respect to cases which we have personally observed as well as those reported in the literature.

The majority of reported cases which have been treated with these agents are those patients to whom the drugs were given prophylactically to prevent extension of a preexisting thrombus, or to prevent clotting in patients believed to be susceptible to intravascular thrombosis. The results of treatment in these cases have been good. Nevertheless, there are still too many patients who develop hemorrhagic complications and too many who discharge emboli to the lungs during and after conclusion of the therapy. Results in patients who were started on treatment following pulmonary infarction have been less encouraging because of the failure of these agents in many instances to prevent subsequent infarctions. We are in agreement

with Ochsner and DeBakey (16), who feel that the use of heparin and dicoumarol in the treatment of pre-existing thrombosis is likely to give the physician a false sense of security. This is particularly true in the treatment of a patient already the victim of pulmonary embolism. However, as a prophylactic measure before thrombosis has occurred, and in the treatment following ligation of the inferior vena cava, these drugs may help to prevent thrombus formation or an extension of the thrombotic process into unaffected vessels. Their value in other conditions associated with intravascular coagulation of blood is acknowledged.

We have also been disappointed in treatment of the disease by proximal venous ligation at levels below the common iliacs. We have personally seen a few patients continue to discharge emboli after ligation was performed bilaterally, and have noted many other examples mentioned in the literature. Veal and Hussey reported 9 cases of postligation embolism. In 4 of these the origin of the embolus was a point in the femoral vein proximal to the site of ligation. Allen and coauthors advocate bilateral femoral vein ligation with phlebotomy and aspiration of the thrombus, if one is present, in the segment of vein to be interrupted. They state, however, that about 5 per cent of their 464 patients had infarcts following this procedure. Some of these were multiple and a few resulted in fatalities. Loewe reported 1 case of fatal embolus after sequential femoral vein ligation and mentioned 4 other patients who continued to throw pulmonary emboli following ligation. Moses, in a very recent report, stated that 2 of his 35 patients with vena caval or iliac vein interruptions were operated upon because of recurrent emboli following bilateral femoral vein ligations. One of these patients died.

Proximal venous ligation at higher levels is apparently the favored procedure at this time over femoral phlebotomy with aspiration of the thrombus. This is due to a greater realization of the danger in leaving even a small portion of thrombus or an area of roughened intima in the vein proximal to the site of its interruption. Such a nidus may become the source of a new propagating thrombus and pulmonary emboli. There seems to be little doubt that the higher the level of the venous ligation, the smaller the risk of recurrent pulmonary embolism. Homans insists that interruption of the femoral vein should always be carried out proximal to the profunda in order to prevent embolism from a thrombus in this vessel. He further states that ligation of the common femoral vein is not as safe as an interruption at a still higher level. He believes that there is usually no thrombus of importance above the external iliac vein, and states that this is an important consideration in common iliac and vena caval interruptions.

Fine and Starr, in commenting upon the effectiveness of venous ligation in preventing embolism, state that, while emboli do occasionally occur following ligation proximal to the thrombus, this phenomenon may be explained in almost every instance on the basis of unilateral ligation or ligation performed at too low a level. For this reason they predict that "vena caval ligation may come to occupy a significant place in the prophylaxis of embolism."

In the surgical treatment of thromboembolism, interruption of the major venous channel from both lower extremities is demanded in the light of present knowledge.

It has been demonstrated pathologically that venous thrombosis in the deep veins of the lower extremities occurs probably more often bilaterally than unilaterally. Fine and Starr state that there is little doubt that in at least half of the patients with the disease both extremities are involved. Hunter and coworkers on the basis of findings in 351 cases published in 1941, found bilateral deep leg vein thrombosis in 110 cases as compared to unilateral involvement in 75 cases. Treatment by proximal venous ligation at any level below the inferior vena cava requires operation bilaterally in order to intercept emboli from both lower limbs. However, in vena caval interruption a *single* operation offers protection not only from emboli arising in the veins of both lower extremities but from a pelvic source as well. Although ligation of the vena cava is a procedure of greater magnitude than femoral vein ligation, we feel that it is often of lesser magnitude than a unilateral iliac vein

ligation. The one major advantage of femoral vein ligations is the fact that local anesthesia may be used satisfactorily, whereas a spinal or general anesthetic is necessary for interruptions of the iliac veins or vena cava. However, the added protection of vena caval ligation against further pulmonary embolism makes it the favored procedure, except in very exceptional cases. Moses has entirely abandoned the iliac approach during the past year in favor of ligation of the vena cava. He states that vena caval interruption "is comparable to ligation of either iliac vein, requiring no more anesthesia, exposure, technical skill or time; indeed, it requires less of each of these factors than does ligation of the left iliac vein, which is short and lies under the aorta."

COLLATERAL CIRCULATION

Second in importance to saving the life of the patient with pulmonary embolism is the consideration of circulatory disturbances in the lower extremities following interruption of their major channels of venous return. Homans has demonstrated anatomically that the collateral circulation following interruption of the common femoral or external iliac vein is far less satisfactory than that following ligation of the common iliac. His own clinical observations and published reports by others are almost uniformly in accord with these anatomic considerations; viz., edema of the extremity is less severe and of shorter duration following common iliac vein ligation than after interruption of the external iliac or common femoral veins. Moses feels that whenever edema has followed ligation of the vena cava or iliac veins there has been unequivocal evidence of either persistence or recurrence of the disease process. It has been pointed out by Homans and more recently emphasized by O'Neil that, in collateral venous circulation, there is no significant choice between placing the ligature about the two common iliac veins or a few centimeters higher about the inferior vena cava.

O'Neil and Weinstein divide the available collateral pathways into three groups which they call the superficial, the deep, and those of the ascending lumbar trunks. The superficial group is composed of the superficial circumflex iliac and superficial epigastric veins which connect the saphenous with the superficial thoracic veins and those of the upper abdominal wall. The deep group is made up of the deep circumflex iliac, superior epigastric and lumbar veins which connect the external iliac with the internal mammary and ascending lumbar veins. The ascending lumbar trunks beginning on either side of the sacral promontory communicate with the sacral, common iliac, hypogastric and iliolumbar veins, and at higher levels with the lumbar veins, the inferior vena cava and right renal vein. The right and left lumbar trunks become the azygos and hemiazygos veins respectively, and ultimately the veins of the azygos system drain into the superior vena cava.

Northway and Buxton (14) have demonstrated the more important collateral channels which function following vena caval obstruction. This was done by means of roentgen studies and dissection following injections of red lead into the femoral veins of cadavers in which the vena cava had been occluded just above the bifurcation. They found that the superior vena cava filled rapidly by way of the ascending lumbars, the segmental veins which associate directly with the vertebral plexuses, through the spinal veins, and above the diaphragm by the azygos system which receives the segmental veins and terminates in the superior vena cava. Important communications between the inferior vena cava and the vertebral systems of veins were found. In all cases there was rapid filling of the inferior vena cava above the obstructed point at the bifurcation. The large internal vertebral plexus on the surface of the dura was well filled with the injected material at the time of laminectomy.

In the light of these findings it was feared that an increased blood flow through the paravertebral venous plexus following ligation of the inferior vena cava might lead to varices in this system with neurological symptoms and signs. However, there have as yet been no cases reported to indicate that this has occurred. Furthermore, Northway and Buxton (14) reported no abnormal findings following

spinal fluid studies for pressure and chemical changes in patients who had had vena caval ligations from two weeks to twelve months previously.

Warren and Weens, in venographic studies using diodrast solution injected directly into the femoral veins of patients having had vena caval ligations, have demonstrated the importance of the ascending lumbar veins, the segmental veins, the vertebral plexuses, the ovarian veins, and veins of the abdominal wall as collateral channels of venous return from the lower extremities. In 1 case recanalization of the inferior vena cava was demonstrated.

INTERRUPTION OF THE VENA CAVA

The earliest recorded cases of complete ligation of the inferior vena cava were those performed because of accidental injury to the vessel during operations upon the kidney. It was soon learned that sudden occlusion of the vessel proximal to the renal veins resulted in death, but it was later found that ligation below the renal veins is compatible with life and health. Northway and Buxton (14) accredit Bottini in 1893 with the first successful ligation of the inferior vena cava. The patient made a complete recovery and suffered no circulatory complications. It was in the treatment of puerperal pyemia that deliberate ligation of the inferior vena cava first gained popularity. The first operations performed in the treatment of this disease are accredited to Trendelenburg, who had his first successful case in 1010. Ochsner and DeBakey (16) mention Krotoski's report in 1037 of 48 successful cases of ligation of the inferior vena cava performed by 27 operators. The majority of these were performed for septic thrombophlebitis resulting from puerperal infection. It is stated that there was no evidence of subsequent circulatory disturbances in the lower extremities of these patients.

In a more recent communication, Ochsner (15) states that Collins, Weinstein, and other members of the gynecologic service at Tulane have ligated the vena cava in 20 cases of severe puerperal pyemia with recovery in all but 1 case. On Ochsner's service the inferior vena cava has been ligated in 3 cases with extensive suppurative thrombophlebitis of the pelvic veins resulting from infections in the lower extremities.

It is only recently that reports of vena caval ligation for deep leg vein thrombosis with and without pulmonary embolism have appeared in the literature. Among recent cases reported in which this operation was performed for pulmonary embolism are 2 by Gaston and Folsom, 3 by Northway and Buxton (14), 6 by Veal and Hussey, 10 by Linton (1), and at least 4 out of a total of 8 cases reported by O'Neil. Moses has recently reported 36 ligations in 35 patients. Fifteen of these were iliac and 21 were vena caval ligations. Twenty-four patients were operated upon for pulmonary embolism.

The inferior vena cava has also been ligated in the treatment of phlebothrombosis without embolism (17), venous clot adherent to the femoral vein and extending into the iliac vein without emboli (12), long-standing phlebitis of both lower extremities (3), and of suppurative femoroiliac thrombophlebitis (9).

To our knowledge, no deaths directly attributable to the operative procedure in the cases of ligation of the inferior vena cava have been reported to date. The majority of patients have had a mild degree of dependent edema in the lower extremities for several months after operation. This is often unilateral and is confined to the limb in which a clinical diagnosis of thrombosis was made before operation. A few have had no clinically detectable edema. In none has the edema been severe or incapacitating. In some cases a femoroiliac thrombophlebitis has developed within a few days following operation. This is commonly unilateral and usually occurs in those patients who showed some clinical evidence of phlebothrombosis in the affected limb before operation. When it occurs it is usually milder and subsides more rapidly than in the average case of phlegmasia alba dolens. No postphlebitic ulcerations have been reported following operation. To our knowledge, there has been no recurrence of pulmonary embolism, fatal or nonfatal, nor have other serious complications been reported subsequent to ligation of the inferior vena cava for thromboembolism.

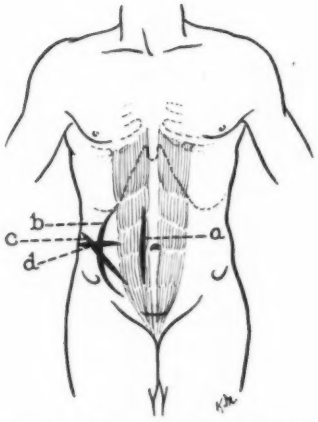

Fig. 1. Incisions commonly used in ligation of the inferior vena cava: *a*, right paramedian, for transperitoneal approach; *b*, *c*, and *d*, incisions for extraperitoneal approach.

THE OPERATION

Ligation of the inferior vena cava is not a difficult operation for those experienced in abdominal and vascular surgery. The primary objective is completely and promptly to interrupt the blood flow from the more distal parts through the vena cava so that emboli arising in these distal veins may not by-pass the point of ligation.

The site of election for ligation is at the level of the aortic bifurcation. This point is immediately above the junction of the left and right common iliac veins to form the inferior vena cava. It is easily found by palpation through the use of the pulsations of the aorta and of the left and right common iliac arteries.

The approach to the inferior vena cava may be either transperitoneal or extraperitoneal. The transperitoneal approach is preferred in cases in which simultaneous ligation of the ovarian veins is indicated, as in pelvic vein thrombophlebitis with pulmonary infarction or pyemia, or in which simultaneous bilateral interruption of the lumbar sympathetic chain seems advisable. Otherwise the extraperitoneal approach is the method of choice. The extraperitoneal procedure is less shocking to the patient and more easily and quickly executed in the majority of patients, and postoperative complications are less frequent than with the transperitoneal approach. Interruption of the right lumbar sympathetic chain may be easily accomplished, if desired, when this approach is used.

Technique. In the transperitoneal approach, a 5 to 6 inch right paramedian incision is preferred (Fig. 1*a*, and Fig. 3). It is made with its midpoint at the umbilicus. The operator in his early experience is usually inclined to make the incision too low unless this landmark is kept in mind. When the peritoneal cavity is entered it is helpful to place the patient in a deep Trendelenburg position. The small bowel is displaced into the upper abdomen and the posterior parietal peritoneum overlying the origin of the inferior vena cava is identified and opened parallel to the course of the vessel for about 2.5 inches. The vena cava is freed from its surrounding connective tissue by careful blunt dissection. Care is taken not to injure tributary lumbar segmental veins which enter the vena cava at its posterolateral aspect on either side. An ordinary blunt-nosed, gall bladder clamp serves admirably for the dissection around the lateral and posterior aspects of the vessel. Two umbilical tape ligatures, placed about 1 centimeter apart, are then passed beneath the vena cava, and the vessel is doubly ligated in continuity.

When there is doubt as to the presence of a thrombus within the vena cava at the point of ligation, this vein may be opened between the two umbilical tape ligatures before they are tied—provided it is clear that no tributaries enter this segment of the vena cava, or if they do, that they are ligated prior to incising the vessel. Traction is maintained on these ligatures to prevent bleeding from below and aspiration of air from above. If a thrombus is found, the patient is placed in a reverse Trendelenburg position, and upon releasing tension on the proximal umbilical tape ligature, suction by means of a glass drinking tube is applied and the clot aspirated. The proximal ligature is then immediately tied. The tension is released momentarily from the distal umbilical tape ligature, and the distal portion of the thrombus, or as much of it as possible, is removed by aspiration. This ligature is then likewise tied securely. Transfixion ligatures of braided silk may be placed between the umbilical tape ligatures as security against the

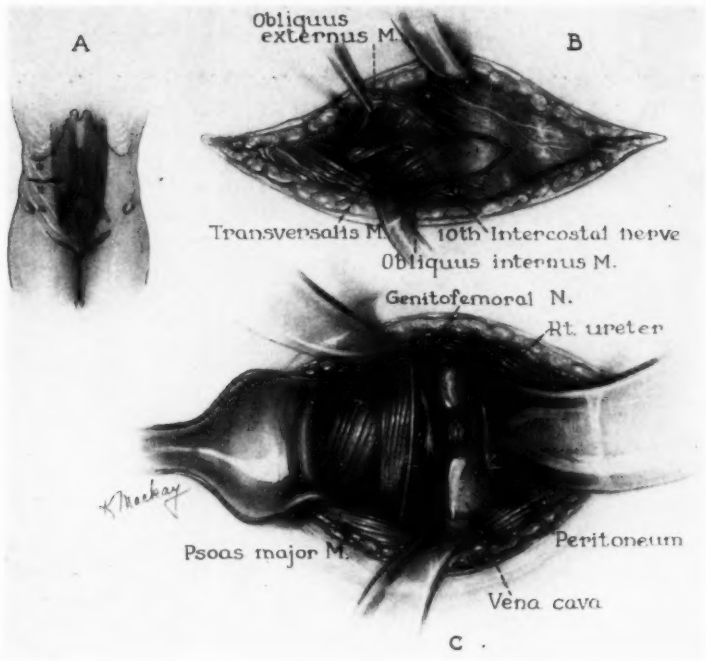

Fig. 2. A, The transverse incision for an extraperitoneal approach to the inferior vena cava is made at or slightly above the level of the umbilicus, from the lateral border of the right rectus muscle to the midaxillary line. B, The external oblique aponeurosis and muscle is cut transversely to a point where further splitting of the muscle upward and outward gives adequate exposure of the internal oblique muscle. The internal oblique and transversus abdominis muscles are split parallel to the course of their fibers and retracted. The 10th and 11th intercostal nerves are spared. C, The peritoneum is bluntly dissected posteriorly and toward the midline to expose the vena cava, the ureter being displaced medially with the peritoneum. The inferior vena cava is ligated just above its origin with two ligatures of umbilical tape placed about 1 centimeter apart.

latter slipping off. This should always be done if the vena cava is completely divided.

If the lumbar sympathetic chains are to be interrupted, they are at this time identified and cut between small silver clips. The right chain is easily found by displacing the vena cava forward and medially. Palpation is a valuable aid in its identity. To reach the left sympathetic chain, it is necessary to dissect retroperitoneally over the aorta and retract it to the right; or the original incision in the posterior parietal peritoneum is closed and another made along the left side of the aorta.

If the left and right ovarian veins are to be ligated, these vessels are identified as near their terminations as possible, and incisions in the posterior parietal peritoneum are made over them.

Closure is carried out in the usual manner, preferably by use of nonabsorbable suture material except in the peritoneum. Care is taken to restore the linea semilunaris.

In the extraperitoneal approach, the patient is placed supine with a folded sheet or thin pillow beneath the right hip and shoulder, so the right side is slightly higher than the left.

A variety of incisions may be used as shown in Figure 1*b*, *c*, and *d*. We have recently begun to use the transverse incision (Fig. 1*d*, Fig. 2A, and Fig. 4) and now prefer it to the others.

We find that it allows excellent exposure with less waste of incision, and since it is made

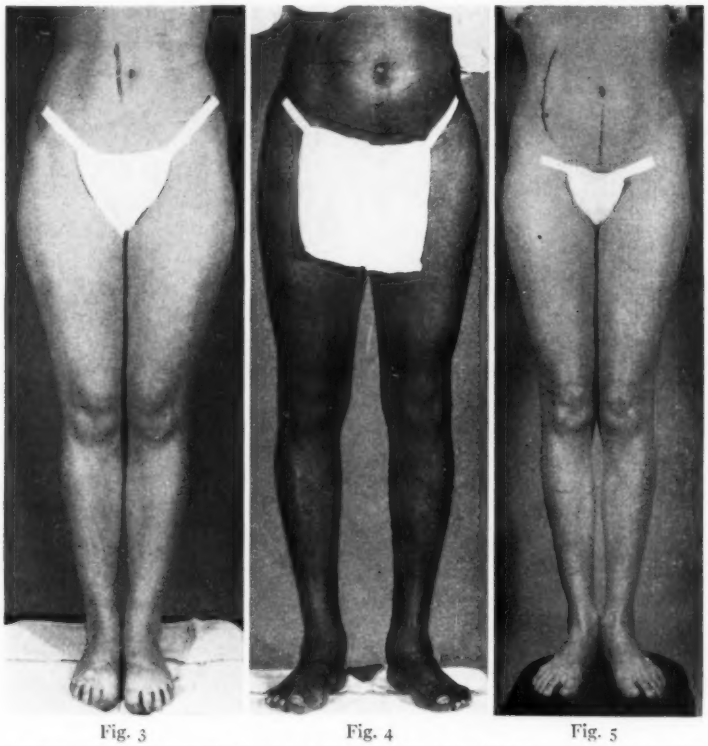

Fig. 3 Fig. 4 Fig. 5

Fig. 3. Case 11, showing the scar of a right paramedian incision. Note the absence of edema 10 months following ligation of the inferior vena cava.

Fig. 4. Case 24, showing the scar of a transverse incision used in an extraperitoneal approach to the vena cava. Photograph showing slight ankle edema was taken 4 months after operation. Six weeks later the edema had cleared completely.

Fig. 5. Case 20. Note the semilunar incisional scar. This patient had a left femoroiliac thrombophlebitis with edema and right deep calf vein thrombosis at the time of pulmonary embolism. Note complete absence of edema 2 months after ligation of the inferior vena cava.

parallel to the natural skin creases, leaves a more pleasing scar. It is made at or slightly above the level of the umbilicus from a point just medial to the lateral edge of the rectus muscle to the midaxillary line (Fig. 2). The incision is extended down to the external oblique. The aponeurosis is incised at the border of the rectus muscle, and the incision is extended about an inch laterally, at which point, as a rule, the muscle fibers can be split further outward and slightly upward to give adequate exposure of the internal oblique muscle (Fig. 2B). The internal oblique and transversus abdominis muscles are then split parallel to the course of their fibers, and the peritoneum is exposed. Should the 10th and 11th intercostal nerves be encountered, they are retracted to avoid injury. The peritoneum is bluntly dissected posteriorly and medially until the vena cava is exposed.

The ureter is identified as the dissection proceeds and is retracted medially, being dissected up with the peritoneum (Fig. 2C). The psoas muscle, the genitofemoral nerve, and the right lumbar sympathetic chain are seen during the course of the dissection.

The point at which the aorta bifurcates is identified by palpation; and at this level the

inferior vena cava is bluntly dissected from surrounding connective tissues, and ligated as described in discussion of the transperitoneal approach.

If indicated, the right lumbar sympathetic chain (Fig. 2C) can be interrupted at this time.

When retractors and packs are removed from the wound, the peritoneum falls back and resumes its normal position, and the split transversus and internal oblique muscles come together to leave very little defect in the abdominal wall.

The incision is closed in layers using nonabsorbable sutures, preferably black silk.

Postoperative care. As with any postoperative patient, treatment following vena caval ligation varies with the problem of the individual. In general, postoperative care is given as for any abdominal surgery.

The pulmonary status of the patient may require oxygen, penicillin or other special attention if there is a considerable area of lung infarcted.

Otherwise, we have found the following measures to be helpful in the postoperative care of these patients:

1. Elastic bandages applied snugly to both lower limbs. These should extend from the base of the toes to the groins, with only the tips of the heels exposed, until the active process in the deep veins subsides. Later the elastic bandages need extend only as high as the tibial tuberosities. They should be worn continuously while the legs are dependent until the patient is ambulatory without edema. In patients who have extensive involvement of the veins of the lower limbs, support may be necessary for from 6 to 12 months. In others with little involvement except in some of the deep calf veins, the use of support for only a few weeks may suffice. Nevertheless, elastic bandage support should be maintained until trial without them reveals no detectable edema following dependency for from 1 to 10 hours.

2. Elevation of the foot of the bed. A 10 to 12 inch elevation of the foot of the patient's bed immediately after operation aids in returning venous blood via the collateral systems of veins from the lower extremities. By speeding up the return flow of blood, this measure may be of value in keeping down extension of the thrombotic process beyond segments of veins already involved. It is helpful in preventing early postoperative edema.

3. Paravertebral lumbar sympathetic blocks with novocain solution. This procedure is of of definite benefit if signs of phlebitis with reflex vasospasm develop postoperatively. It is performed unilaterally or bilaterally as indicated, and is repeated daily until all evidence of vasospasm disappears.

4. Prostigmin 1:2,000 solution. We have used this drug in doses of 1 cubic centimeter subcutaneously every 3 hours to prevent abdominal distention, to aid voluntary urination, and to help prevent further intravascular clotting of blood (4).

5. Heparin and dicoumarol. These drugs may be used postoperatively, preferably in combination, as prophylaxis against propagation of thrombi in the veins of the lower limbs or in the branches of the pulmonary artery. In this series we have used them in only 1 patient (Case 34) who had recurrence of pleuritic pain 48 hours after operation.

(We have consistently noticed that all patients in our series who had severe pleuritic pain for varying periods of time prior to ligation of the vena cava were completely relieved of this pain upon reacting from the anesthetic. This fact has led one of us (B.R.T.) to feel that perhaps the pleuritic pain produced by a single pulmonary embolus is of rather brief duration, possibly 1 to 6 hours, and that many patients in whom the pain persists for longer periods are actually having repeated pulmonary embolizations. Two patients in this series had postoperative recurrence of pleuritic pain. In these cases the pain was probably due to peripheral propagation of thrombi from points of previous embolic occlusions of branches of the pulmonary artery.)

6. Ambulation. The patient is encouraged to become ambulatory as soon as possible after operation. The length of time depends upon the degree of pulmonary damage and clearing of the infarcted areas; upon the status of the phlebitis and/or edema of the lower extremities; and upon the general condition of the patient. In the absence of infection and in the presence of a positive protein balance, the operative wound is not considered as a factor

TABLE I.

Case No. Patient Hospital No.	Age Race Sex	Site of thrombosis	Date of operation	Approach	Sympathetic interruption	Postoperative complications	Immediate effects	Length follow-up period Months	Later effects		Remarks
							Thrombophlebitis Edema		Pain Edema	Varicosities	
1 C. G. 234842	24 Colored Female	Bilateral femoroiliac	9–22–43	Transperitoneal	No	Incisional hernia	None 1 plus	33	None None	None	Hernia has subsequently been repaired Patient is well and has no complaints.
2 H. D. A104116	34 White Female	Left femoroiliac	10–14–44	Transperitoneal	Bilateral	None	Increased 2 plus	17	None 1 plus, right	None	Patient has slight dependent edema in the right leg after prolonged standing. Edema not apparent in early morning.
3 J. D. C. A108079	31 White Male	Right deep calf	3–20–45	Transperitoneal	No	Incomplete intestinal obstruction	Increased 1 plus	13	None None	None	
4 B. F. 214411	39 Colored Male	Bilateral femoroiliac	3–29–45	Transperitoneal	No	None	Increased 3 plus	13	Cramps None	None	Patient is a window washer on feet 10 hours per day.
5 J. C. 262966	32 Colored Male	Bilateral deep calf	4– 8–45	Transperitoneal	No	Died 5 hours postoperative					Patient died 5 hours after operation. Autopsy revealed acute cor pulmonale and multiple bilateral pulmonary infarcts.
6 G. L. A109224	29 White Male	Left deep calf	4–18–45	Transperitoneal	No	None	Increased 2 plus	3	None 1 plus	None	Patient has slight dependent ankle edema after prolonged standing. Edema not apparent in the early morning.
7 J. H. 137–875	41 White Male	Bilateral femoroiliac	4–25–45	Transperitoneal	No	None	None 2 plus	13	None None	None	
8 W. C. A8742	13 White Female	Bilateral femoroiliac	5– 3–45	Transperitoneal	No	None	Increased 1 plus	11	None None	None	
9 H. M. 204519	40 Colored Female	Silent	5–24–45	Transperitoneal	No	None	Increased 4 plus right; 1 plus left	5	None 1 plus	None	Patient has slight dependent ankle edema after prolonged standing. Edema not apparent in the early morning.
10 W. B. 213754	35 Colored Male	Right femoroiliac, Left deep calf	5–30–45	Transperitoneal	No	None	Increased 3 plus left	3	None None	None	
11 A. M. A101355	20 White Female	Left femoroiliac	6–29–45	Transperitoneal	No	None	None 1 plus	11	None None	None	
12 N. K. A67674	35 White Female	Bilateral deep calf	6–29–45	Transperitoneal	Right	Complete obstruction jejunum	None None	11	None None	None	Obstruction relieved surgically 3 weeks after vena caval ligation. Patient now employed as a saleslady, and is on her feet over 8 hours a day.
13 L. J. 137624	32 Colored Female	Silent	7–25–45	Transperitoneal	No	None	None None	8	None None	None	

TABLE I.—Continued

Case No. Patient Hospital No.	Age Race Sex	Site of thrombosis	Date of operation	Approach	Sympathetic interruption	Postoperative complications	Immediate effects	Length follow-up period Months	Later effects		Remarks
							Thrombophlebitis Edema		Pain Edema	Varicosities	
14 M. V. A80913	22 White Female	Bilateral deep calf	8–16–45	Extraperitoneal	No	None	None None	8	None None	None	Patient is a graduate nurse on full hospital duty, standing over 8 hours per day.
15 N. S. 276428	36 Colored Female	Left deep calf	9– 6–45	Extraperitoneal	No	None	Increased 1 plus	6	None None	None	
16 F. G. 212289	21 Colored Female	Left femoro-iliac	9– 9–45	Extraperitoneal	No	None	Increased 4 plus	6	None None	None	
17 F. C. 151–614	28 White Female	Bilateral femoro-iliac	9–13–45	Transperitoneal	Bilateral	None	Increased 1 plus	11	None None	None	
18 H. K. 152–233	52 White Male	Left femoroiliac, Right deep calf	10– 7–45	Transperitoneal	Bilateral	None	Increased 2 plus except right	5	None 2 plus, left	None	Patient has slight persistent edema, more marked on prolonged standing. Patient was a left hemiplegic before operation, and edema is confined to the paralyzed lower limb.
19 C. B. 157748	53 Colored Male	Silent	11–21–45	Extraperitoneal	No	None	Increased 4 plus	4	None 1 plus	None	Patient has slight dependent ankle edema after prolonged standing. Edema not apparent in the early morning.
20 L. K. 155–243	23 White Female	Left femoroiliac, Right deep calf	1–10–46	Extraperitoneal	No	None	None None	6	None None	None	Patient has a full time job, standing over 8 hours per day.
21 J. A. 280405	30 Colored Male	Right deep calf	1–28–46	Extraperitoneal	No	None	Increased 4 plus	6	None 1 plus	None	Patient has slight dependent ankle edema after prolonged standing. Edema not apparent in the early morning.
22 C. W. 232564	35 Colored Male	Silent	1–30–46	Extraperitoneal	No	None	Increased 2 plus, right	2	None 2 plus	None	Patient has slight persistent edema, more marked on prolonged standing.
23 A. J. 190046	49 Colored Male	Silent	1–29–46	Extraperitoneal	No	Wound infection	None None	2½	None None	None	
24 M. B. 257840	25 Colored Female	Bilateral femoro-iliac	2– 7–46	Extraperitoneal	Right	None	None 1 plus	5½	None None	None	Patient is a student nurse on full duty.
25 W. J. 156–376	27 White Male	Left deep calf	2–20–46	Extraperitoneal	No	None	None None	2	None None	None	Patient is still confined to bed with fracture dislocation of left hip.
26 E. D. 157–007	47 White Female	Bilateral deep calf	3–23–46	Transperitoneal	Bilateral	None	Increased 3 plus	2½	None None	None	Two days postoperatively the patient had a recurrence of the pleuritic pain experienced prior to operation. She recovered without specific therapy. It was the clinical impression that a peripheral extension of the original pulmonary embolus occurred. Patient is now a store clerk on feet 10 hours a day

TABLE I.—Continued

Case No. Patient Hospital No.	Age Race Sex	Site of thrombosis	Date of operation	Approach	Sympathetic interruption	Postoperative complications	Immediate effects	Length follow-up period Months	Later effects		Remarks
							Thrombophlebitis Edema		Pain Edema	Varicosities	
27 L. H. A122514	34 White Female	Bilateral deep calf	4- 4-46	Extraperitoneal	No	None	None None	3	None 1 plus	None	Patient has slight dependent ankle edema after prolonged standing. Edema not apparent in the early morning.
28 M. E. A115737	18 White Female	Bilateral femoroiliac	4-27-46	Extraperitoneal	No	Severe pharyngitis and otitis media	None None	3	None None	None	
29 A. M. 56427	45 Colored Female	Left femoroiliac	6-20-46								Prior to operation respiratory rate 40 per minute. Patient had almost constant cough productive of bright bloody sputum. Was in mild cardiac failure. Died during induction of anesthesia. No autopsy.
30 L. H. 285632	21 Colored Male	Silent	6-29-46	Extraperitoneal	No	None	Increased 1 plus				
31 W. M. A119234	64 White Male	Right femoroiliac above point of ligation of superficial femoral vein.	7- 6-46	Extraperitoneal	No	None	Increased None				Patient had recurrence of pulmonary embolism following ligation of both superficial femoral veins for embolism apparently arising from bilateral deep calf vein thromboses.
32 W. R. 214204	34 Colored Male	Bilateral femoroiliac	7- 9-46	Extraperitoneal	No	Died 20 minutes after operation					Patient died 20 minutes after closure of incision. Autopsy revealed a large embolus completely occluding the left pulmonary artery. Pathologist's opinion was that this occurred prior to operation.
33 H. C. McCall Hosp., Rome, Ga.	44 White Male	Silent	7-18-46	Extraperitoneal	No	None	None None				
34 A. J. 101-172	67 White Male	Bilateral deep calf	7-24-46	Extraperitoneal	Right	None	Increased Right				Patient continued having clinical and x-ray findings of extension of original embolus after operation. Treated with heparin and dicoumarol.
35 J. O. 75282	38 Colored Male	Silent	8- 7-46	Extraperitoneal	No	None	None None				
36 J. J. 161-625	71 White Male	Silent	8- 8-46								Patient probably had repeated pulmonary embolism over a period of 6 months. He died suddenly on the operating table 20 minutes after anesthesia was begun. Permission for autopsy was refused.

in determining when to permit the patient to leave his bed.

PRESENTATION AND DISCUSSION OF CASES

Of the 36 cases reported, 34 were treated for pulmonary embolism by ligation of the inferior vena cava. The pertinent data on these patients are recorded in Table I. The other 2 died on the operating table before the vena cava was ligated.

One incisional hernia and 2 intestinal obstructions, 1 complete and 1 incomplete, developed postoperatively. In these 3 cases the transperitoneal approach was used. Other postoperative complications consisted of 1 wound infection and 1 case of pharyngitis and otitis media.

No attempt has been made to differentiate between thrombophlebitis and phlebothrombosis, since the purpose of the paper is to treat only the matter of procedure once pulmonary embolism occurs from the legs or pelvis, regardless of the primary disease. All of the patients had had at least one episode of pulmonary embolism, and some more than one. Prophylactic ligation before embolism was not done in any case.

Seventeen of the patients were colored and 19 were white. Seventeen were females and 19 were males. The age incidence showed the majority to be between 21 and 40 years of age. It is noteworthy that 3 of these patients were between 10 and 20 years of age; 10 between 21 and 30; and 5 above 50 years of age.

In this small series, little correlation between the clinical location of the thrombosis and the occurrence of pulmonary embolism was apparent. Eight patients were afflicted with bilateral femoroiliac disease; 6 with bilateral deep calf vein thrombosis; 3 with femoroiliac disease on one side and deep calf vein thrombosis on the other; 5 with femoroiliac disease on one side and no clinical evidence of disease on the other; 5 with only unilateral deep calf vein thrombosis; and 9 patients showed no clinical findings suggestive of disease in either lower extremity.

Results have been classified under two general headings: immediate effects and late effects. Immediate effects should be taken to mean the changes occurring within 10 days after the operation. Within this period, 14 showed no effect on the thrombophlebitis; neither pain, temperature, nor tenderness was increased. Eighteen showed definite aggravation of the disease. Immediately after operation the edema increased in 20 but 12 showed no increase. These findings are especially interesting in view of the fact that vena caval ligation has been performed therapeutically for chronic thrombophlebitis with edema.

All patients were seen for later follow-up studies. The length of time elapsing between operation and last observation varied between 33 months and 2 months. Late effects on some of the living patients have not been recorded since the time lapse has been too short. Twenty-six patients have no pain. One patient has occasional cramping pains in the calves of the legs. Twenty-seven patients have no varicosities. No edema is apparent in 19 patients (Figs. 3 and 5), 6 patients have slight dependent edema after standing all day, and 2 patients have slight persistent edema. In none is the edema incapacitating. It is doubtful whether the edema in this series of cases is any greater than would have been anticipated had not vena caval ligation been performed.

Lumbar sympathectomies were done at the time of vena caval ligation on 7 of the cases. Four of these operations were performed bilaterally, and 3 were confined to the right side. In 6 of these cases the disease intensified clinically as evidenced by an increase in pain or tenderness; or there was an increase in edema. It is interesting to note that in Case 34, with bilateral deep calf vein thrombosis, there was a transient increase in calf pain on the side upon which the lumbar sympathetic chain was interrupted.

Four patients died. Of these, Patient 5 died 5 hours after the operation. Autopsy revealed an acute cor pulmonale and multiple bilateral pulmonary infarcts. Patients 29 and 36 died on the operating table before vena caval ligation was effected. Patient 29 was a cardiac in mild failure at the time of operation, and both patients had had several episodes of pulmonary embolism. Autopsies were not obtained on these 2 cases. Patient 32 died 20 minutes after closure of the incision. Autopsy

revealed a large embolus completely occluding the left pulmonary artery. Apparently these patients do not tolerate surgery well if operation is delayed until after massive pulmonary infarction has occurred. Vena caval ligation is advocated as soon as possible, therefore, after the first embolism has occurred. Case summaries with brief comments on the patients who died are given below.

Forty-eight hours after operation Patient 34 experienced increased chest pain. Patient 26 had a similar episode of pain 48 hours postoperatively. She recovered completely without specific therapy. It was assumed that there had been an extension of an embolus lodged in a branch of the pulmonary artery prior to operation in both of these cases. In Case 34, it is interesting to note that although the patient was placed on heparin and dicoumarol at the time of recurrence of the pain, 7 days later he again suffered from an acute exacerbation of pain in spite of a decrease in prothrombin to a level ranging between 15 and 30 per cent of normal. This gradually subsided, and since that time he has had no further chest pain. X-ray studies confirmed the impression that no new areas of pulmonary infarction were present. None of the patients showed evidence of any new pulmonary embolism after vena caval ligation.

Since many writers are advocating bilateral ligation of the femoral veins above the site of thrombosis as treatment of pulmonary embolism, Patient 31 merits special note. Both femoral veins were simultaneously ligated after pulmonary embolism had developed, with evidence of bilateral deep calf vein thrombosis. Subsequently, the patient suffered a new embolus. The vena cava was ligated and the patient made an uneventful recovery. During the past year the writers have had 2 patients (unreported) die from fatal emboli subsequent to bilateral femoral vein ligations for deep calf vein thrombosis with pulmonary embolism.

SUMMARIES OF FATAL CASES

CASE 5. J. C., Hospital No. 262966, a 32 year old colored male, was admitted to the Medical Service of Grady Memorial Hospital on March 29, 1945 for severe congestive heart failure. One year previously he had developed cardiac decompensation and treatment was given in the out-patient department. Despite treatment he became severely decompensated in March, 1945. Response to bed rest, diuresis, and the removal of 900 cubic centimeters of clear amber fluid from the right pleural cavity in addition to digitalis was good. The patient's weight dropped from 177 to 155 pounds by the 5th hospital day. On April 4, 1945, the 7th hospital day, he suddenly developed severe pain in the lower right anterior chest. This pain was inadequately relieved by intercostal nerve block with novocain solution. An x-ray film of the chest on the following day revealed a density in the right cardiophrenic angle consistent with a pulmonary infarction. The lower extremities were negative for any signs suggesting phlebitis until April 8, 1945, the 11th hospital day, when both calves became tender to pressure and Homans' sign became positive bilaterally. Femoral vein tenderness was also noted at this time. By this time the patient's general condition had gone rapidly downhill from repeated episodes of pulmonary embolism. Since it was obvious that death was certain unless the emboli were interrupted, the patient was prepared, and with the use of spinal anesthesia (15 mg. of pontocaine), the inferior vena cava was ligated following a transperitoneal approach. The patient stood the procedure well, but 5 hours after conclusion of the operation he died suddenly. An autopsy was performed, and pathologic studies revealed multiple, bilateral, pulmonary infarctions, acute cor pulmonale, luetic aortitis and valvulitis with aortic insufficiency. It is believed that the patient's death resulted from acute failure of the right side of the heart due to massive embolic obstructions of the pulmonary arterial tree.

Several mistakes in the management of this patient are now obvious. No treatment, except symptomatic, was given for pulmonary embolism until 4 days after its onset; vena cava ligation was carried out transperitoneally in a patient critically ill. It is interesting to note that this cardiac patient had no signs of venous disease in the lower limbs until almost dead of pulmonary infarctions; and that when signs developed in the calves, the femoral veins were noted to be tender as high as the inguinal ligaments, indicating that thrombi had already propagated to the external iliac veins.

Should we face the same problem today, we would ligate the inferior vena cava extraperitoneally as soon as the diagnosis of pulmonary infarction had been made, irrespective of an absence of signs of venous disease in the lower limbs, and regardless of the comparatively small possibility of the heart itself serving as a source for the pulmonary emboli. If,

following ligation, there should be recurrence of pleuritic chest pain in the same or in a different location, heparin and dicoumarol would be started immediately. It is possible that this patient would be living today had this plan of treatment been followed.

CASE 29. G. McC., Hospital No. 56427, a 45 year old colored female, was first seen in the surgical outpatient clinic, Grady Memorial Hospital, on June 6, 1946. She complained of pain and swelling in the left upper thigh. Examination revealed edema and tenderness in the region of the femoral vessels in the upper left thigh. There were no signs of phlebothrombosis in either leg. A diagnosis of cellulitis was made by the examining interne. Bed rest at home and sulfadiazine were prescribed. The patient returned on June 20, 1946 and was admitted to the hospital on the surgical service. She stated that on the previous night she experienced a sudden severe pleuritic pain in the right chest which persisted. On the morning of admission she developed hemoptysis. Examination revealed an acutely ill patient who was dyspneic and coughing up large amounts of bright red blood. Temperature was 98.6, pulse 110, respiration 40, blood pressure 180/120. The heart was moderately enlarged to the left. Physical signs of consolidation of the lower lobe of the right lung with friction rub were present. X-ray examination of the chest suggested pulmonary infarction of the right lower lobe. There was a 2 plus pitting edema of both legs and feet, and tenderness along the course of the left femoral vein was noted. There was no calf tenderness, and Homans' sign was negative bilaterally. Upon the recommendations of the medical consultant, rapid digitalization with lanatosid C was started 2 hours after admission to the ward, and a mercurial diuretic was given intravenously. One hour later the patient was transported to the operating room for ligation of the inferior vena cava. Within 5 minutes after beginning the administration of nitrous oxide and oxygen to induce anesthesia, the patient had a sudden respiratory arrest which could not be overcome. Autopsy permit was refused.

The cause of death in this patient was probably a massive pulmonary embolus which occurred during induction of the anesthesia, since respirations ceased so abruptly and preceded cardiac standstill by a few moments. However, we cannot definitely rule out anoxia as playing an important rôle, in view of the large area of pulmonary tissue already disabled by previous infarctions, plus the limited amount of oxygen permitted with nitrous oxide induction.

Obviously this patient needed emergency treatment in an effort to save her life. She had been throwing emboli for less than 24 hours at the time of her death, and this fact, plus the physical and x-ray findings upon admission to the hospital, suggested that large emboli were being discharged, probably from a left femoroiliac venous thrombosis. Femoral ligations therefore were felt to be out of the question. Iliac or vena caval ligation seemed indicated. Since local anesthesia is unsatisfactory for either of these procedures, a general or a spinal anesthetic was necessary. Because of the marked hypertension, a general anesthetic was preferred.

It seems that inhalation anesthetic agents with which adequate oxygen is given will prove to be the safer for vena caval ligation, especially in patients with extensive pulmonary infarction.

CASE 32. W. R., Hospital No. 214204, a 45 year old colored male, was admitted to the medical service of Grady Memorial Hospital on July 9, 1946. Three weeks previously the patient had developed superficial ulcerations on both shins accompanied by edema of the legs, feet, and ankles. The ulcers had healed and the swelling had almost completely subsided. The history did not suggest the cause of the ulcerations, but since the patient was totally blind, it was believed that they were traumatic in origin. The patient was otherwise well until 2 days prior to admission, when he developed a dull, aching pain in the lower left anterior chest which soon came to resemble pleurisy. The onset of pain was accompanied by a cough which was productive of mucoid sputum. Both symptoms persisted. On the day of admission he began coughing up bright red blood. Physical examination revealed temperature to be 102.6, pulse 120, respiration 42, blood pressure 105/70. The patient was orthopneic and appeared acutely ill. There were signs of lung consolidation in the left lower lobe posteriorly, and some evidence of free fluid in the left pleural space. Thoracentesis yielded 50 cubic centimeters of old and fresh serosanguinous material. The lower extremities revealed a 1 plus pitting edema of the legs and feet. The left calf was slightly larger than the right. There was no tenderness along the course of the femoral or popliteal veins nor tenderness to compression of the calf muscles. Homans' sign was negative bilaterally. An x-ray study of the chest showed a pleural effusion on the left with shift of the mediastinum to the right.

For reasons unknown, the patient received no treatment whatever until 12 hours after admission to the hospital, when a preoperative hypodermic was administered. Shortly thereafter he was taken to the operating room. Under spinal anesthesia supplemented with local infiltration of 1 per cent novocain solution and sodium pentothal intravenously, the inferior vena cava was ligated through a right lumbar incision by an extraperitoneal approach. The

patient went into shock as the muscle layers of the abdominal wall were split for exposure of the peritoneum. In spite of blood plasma and other measures to combat the circulatory collapse, he failed to respond and died a few minutes after conclusion of the operation.

It was the clinical impression at the time that the patient's circulatory collapse resulted from a large pulmonary embolus which was thrown off prior to interruption of the inferior vena cava.

Autopsy revealed a large embolus completely occluding the left main branch of the pulmonary artery, and massive infarction of the lower lobe of the left lung. Small adherent thrombi were found in the prostatic plexus of veins. No premortem clots were demonstrated in the iliac veins. Permission for exploration of the large veins below the inguinal ligaments was not granted.

Had operation been carried out promptly upon admission to the hospital, it is possible that this patient would have survived, since his death was apparently the result of recurrent pulmonary embolism. Although the source of the emboli was not demonstrated at autopsy, it is probable that they arose from thrombi in one or both femoral veins.

CASE 36. J. J., Hospital No. 161–625, a 71 year old white male, was first seen in February, 1946, complaining of dyspnea and retrosternal fullness of sudden onset. Examination revealed a blood pressure of 130/80. The heart was slightly enlarged and there was a harsh systolic murmur at the apex. Numerous moist râles were heard in the lower lobe of the right lung. There was a slight edema of both feet. The dyspnea disappeared following an intravenous injection of a mercurial diuretic. X-ray examination of the chest 4 days later revealed a small pleural effusion on the left and a small area suggestive of infarction in the left lower lobe.

His condition remained satisfactory until April 8, 1946, when there was an acute recurrence of dyspnea. Examination revealed moist râles at the left lung base, distention of the neck veins and cardiac fibrillation. He responded as before to the same treatment. Four days later the dyspnea recurred, and he developed a cough productive of mucopurulent sputum. He continued to have dyspnea intermittently. The lower extremities remained conspicuously negative for signs of phlebitis.

On June 15, 1946 the patient developed hemoptysis. X-ray examination of the chest showed a partial atelectasis of the right upper and lower lobes. It was the clinical impression at that time that the patient had a bronchogenic carcinoma. He was hospitalized for roentgen therapy. There was roentgenological evidence of improvement of the atelectatic process after several weeks.

On August 8, 1946 he developed areas in the left lung suggestive of pulmonary infarctions. A surgical consultation was requested at this time. In view of the x-ray evidence of pulmonary infarctions, it was decided to ligate his inferior vena cava although his lower extremities remained negative.

He received 0.75 gram of sodium pentothal intravenously as an induction agent. Following this he was given nitrous oxide, oxygen, and ether. A transverse skin incision was made and the external oblique muscle was divided. At this point, respiration and pulse stopped suddenly, and the patient failed to respond to stimulants and artificial respiration. Permission to perform an autopsy was not obtained.

The cause of death in the patient remains unexplained. It is possible that he had a massive pulmonary embolus on the operating table. On the other hand, he had been sick for 6 months and was a poor surgical risk. This case serves to emphasize the suggestion that if the vena cava is to be ligated, it should be done as soon as possible after the first embolus is recognized.

In retrospect, the question has arisen as to whether or not this death was due to a poor choice of anesthetic agents. It is felt that sodium pentothal is not the safest anesthetic for elderly or poor risk patients.

SUMMARY AND CONCLUSIONS

1. The importance and significance of thromboembolism and the various methods of treatment are discussed.

2. The advantages of ligation of the inferior vena cava are presented.

3. The operative technique of vena caval ligation is described in detail.

4. Thirty-six cases of thromboembolism are reported. In 34 patients ligation of the inferior vena cava was performed. Two patients died on the operating table before ligation could be accomplished. There was no known recurrence of pulmonary embolism in any of the patients operated upon.

5. Follow-up studies are presented.

6. Ligation of the inferior vena cava is recommended as the treatment of choice in patients with thromboembolism.

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TOTAL GASTRECTOMY

Report of 89 Cases

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SINCE the first report of a total gastrectomy in 1884 more than 300 have been reported in the literature. In 1943 Pack and McNeer collected all of the published reports, of which there were 283 operations, and added 20 of their own. In this study the outstanding facts were the high operative mortality and the few instances of long survival. That these should be the outstanding features was to be expected from the nature of the lesions for which this procedure is required and the relative inexperience with which surgeons of necessity operated.

In 1927 the first total gastrectomy was performed at the Lahey Clinic and 88 additional operations had been done by October 1, 1945. Since there have been few reports (2, 3) of a large number of cases from any one clinic, the information gained from these 89 operations seems worthy of presentation.

CRITERIA FOR SELECTION OF CASES

The history of the patient was more or less nonspecific and offered little assistance in determining the need for total gastrectomy. In every case, however, there was roentgenologic evidence of a lesion involving the stomach. In many, the lesion was extensive; in others, although localized, the cardia or the lower end of the esophagus or both were known to be involved preoperatively. A fixed lesion or involvement of additional sites in the small intestine or colon demonstrable by roentgenologic examination, a mass palpable in the epigastrium, palpable nodules in the liver, a supraclavicular node, or a rectal shelf, were considered to be contraindications to exploration (1).

In some instances, the necessity for total gastrectomy was not realized until the stomach was examined at the time of operation. Careful exploration under the direct vision of an abdominal approach provided the most satisfactory determination of the extent of the lesion, the presence of local or distant abdominal metastases and, consequently, the advisability of attempting the operation. The paper by Lahey and Marshall gives detailed indications for total gastrectomy.

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AGE AND SEX DISTRIBUTION

In this series there were 51 male patients and 38 female patients. The youngest was 23 years of age and the oldest 75. The age distribution is shown in Table I. There were 2 patients in the third decade and 11 who were 70 years of age or over, of whom 3 were 75. In this latter group, 5 patients survived the operation, 1 of whom lived for 2 years and 1 is still alive 18 months after operation. Although the largest number of patients fell within the age range of 40 to 70 years, it is important to remember not only that patients less than 40 years of age (10 per cent in this series) may develop lesions necessitating total gastrectomy but also that an age of 70 or greater is not a contraindication to this extensive procedure.

SYMPTOMATOLOGY

The duration of symptoms from the time of their onset until the patient was first seen at the Clinic is shown in Table II. In more than half of the patients this was 6 months or less and in one-fourth it was 3 months or less. This should serve to emphasize the necessity for prompt and thorough investigation of any patient with gastrointestinal complaints and to condemn the far too prevalent practice of symptomatic treatment until the patient develops unmistakable evidence of disease.

The most common presenting symptoms in these patients are listed in Table III. Examination of this table shows that there is no suggestive symptom or syndrome. Unexplained loss of weight in patients with digestive com-

TABLE I.—AGE DISTRIBUTION—89 PATIENTS

Age, years	No. patients
20–29	2
30–39	7
40–49	19
50–59	26
60–69	24
70–79	11

TABLE II.—DURATION OF SYMPTOMS WHEN FIRST SEEN

No. months	No. patients
3 or less	23
4 to 6	23
7 to 9	8
10 to 12	13
13 to 18	5
19 to 24	5
25 to 36	5
37 to 48	2
Over 48	1
Unspecified	4

plaints suggests a malignant lesion in the gastrointestinal tract. Loss of weight occurred in 66 patients of this series (Table IV). In 28 the loss was more than 20 pounds. Twenty-two had gastric fullness and pressure, 8 had an ulcer syndrome, 8 diarrhea, 6 dysphagia, indigestion, and heartburn. All of these symptoms indicated disturbance in gastrointestinal function but none could be considered specific for a gastric lesion. These self-evident facts are mentioned to stress the point that although a careful history may in some instances lead to a correct diagnosis, in many the complaints are so nonspecific and even apparently unimportant that the diagnosis may be missed or delayed until too late for successful surgical intervention unless the insidious symptomatology is constantly borne in mind.

CLASSIFICATION OF LESIONS

There were 88 malignant tumors, 2 benign tumors which were leiomyomas, and 3 nonneoplastic lesions, of which 2 were chronic gastritis and 1 showed multiple ulcers. The malignant tumors consisted of 81 carcinomas of which 48 were carcinoma simplex and 25 adenocarcinoma, 4 sarcomas, of which 3 were lymphosarcomas and 1 a leiomyosarcoma, and 3 lymphomas. Of the latter, 2 were classified as Hodgkin's disease and 1 as malignant lymphoma. The pathologic classification of all the lesions is given in Table V.

TABLE III.—PRESENTING SYMPTOMS

	No. patients
Loss of weight	66
Pain	47
Anorexia	27
Nausea and/or vomiting	26
Weakness and fatigability	25
Epigastric fullness and pressure	22
Constipation	14
Ulcer syndrome	8
Melena	8
Diarrhea	8
Dysphagia	6
Interscapular pain	6
Dyspepsia, indigestion, heartburn	5
Regurgitation	5
Gaseous distention	5
Hematemesis	4
Belching	3
Pallor	2
Chest pain	2
Back pain	2
Other complaints—Ribbon-like stools, intolerance to liquids, ankle edema, sitophobia, depression, tetany, headaches, and numbness of feet	1 each

As has been pointed out by Lahey and Marshall, carcinoma of the stomach may be readily divided into two types: one the localized type which rapidly metastasizes to adjacent lymph nodes and the other the linitis plastica or leather-bottle type in which the carcinomatous infiltration spreads through the muscle bundles in the gastric wall, and makes a rigid but comparatively rarely metastasizing lesion which is appropriate for total gastrectomy.

The infiltrative and slowly metastasizing properties of lymphosarcoma also make the patient with this malignant growth a good risk for total gastrectomy. Patients with low grade malignant and benign lesions causing esophageal obstruction at the cardia also have yielded good results with this operation.

PREOPERATIVE BLOOD STUDIES

Much has been written about the effect of malignant disease of the stomach on the blood

TABLE IV.—WEIGHT LOSS PREOPERATIVELY

No. pounds	No. patients
10 or less	10
11 to 20	19
21 to 30	18
31 to 40	3
41 to 50	6
Over 51	1

Fifty per cent of patients on whom information is known lost 20 pounds or more.

TABLE V.—CLASSIFICATION OF LESIONS

	No. cases	Total cases
Malignant tumors		
Carcinoma—81		
Adenocarcinoma	25	
Adenoacanthoma	2	
Carcinoma simplex	48	
Epidermoid carcinoma	2	
Adenocarcinoma with mucinous foci	1	
Unclassified	3	
Sarcoma—4		
Lymphosarcoma	3	
Leiomyosarcoma	1	
Lymphoma group—3		
Lymphoma	1	
Hodgkin's disease	2	
Total malignant tumors		88
Benign tumors		
Leiomyoma	2	
Total benign tumors		2
Nonneoplastic lesions		
Chronic gastritis	2	
Multiple peptic ulcers	1	
Total nonneoplastic lesions		3

picture. Since the majority of these lesions were malignant, the findings of the preoperative blood studies are presented as a whole in Table VI. In 78.8 per cent the red blood cells numbered 4,000,000 or more. In 59.5 per cent the hemoglobin was 13 grams or less. It is of interest to note that in a significant number of

TABLE VI.—PREOPERATIVE BLOOD STUDIES

Red blood cell counts*	
1 to 2 million	1
2 to 3 million	2
3 to 4 million	14
4 to 5 million	49
5 to 6 million	14
Hemoglobin determinations†	
Less than 6 grams	1
6 to 8 grams	4
8 to 10 grams	13
10 to 12 grams	15
12 to 14 grams	25
Over 14 grams	26
White blood counts‡	
Less than 5,000	7
5,000 to 7,000	27
7,000 to 9,000	17
9,000 to 11,000	16
Over 11,000	14

*78.8% of counts were 4 million or greater.
†40.5% of determinations were 13 grams or greater.
‡21% of counts are less than 6,000; 42% are between 6,000 and 9,000; 37% are greater than 9,000.

TABLE VII.—DEGREE OF ACIDITY IN PREOPERATIVE ANALYSES

	No. cases
No free hydrochloric acid	42
Less than 25 degrees	11
25 to 50 degrees	6
Greater than 50 degrees	2

68.9% of analyses showed anacidity.
89.6% of analyses showed acidity of 25 or less.

cases no anemia, or anemia of a mild degree was present. The general trend was toward hypochromia and even in those cases in which severe anemia was present a macrocytic hyperchromic type was a rarity.

There was no characteristic picture in the number of white blood cells. The counts varied from 3,050 to 16,800. In 21 per cent the counts were less than 6,000, in 42 per cent between 6,000 and 9,000, and in 37 per cent they were greater than 9,000.

PREOPERATIVE GASTRIC ACIDITY

The degree of gastric acidity preoperatively is shown in Table VII. No free acid was found in 68.9 per cent and in 89.6 per cent it was 25 units or less. A comparison of this series with a group of Lahey Clinic patients subjected to subtotal gastrectomy for carcinoma of the stomach shows a greater incidence of anacidity or low acidity in patients requiring total gastrectomy. On the other hand, it is important to realize that an acidity of 50 units or greater is not incompatible with a lesion for which total gastrectomy is necessary. Unless this is constantly borne in mind, a sense of false security may result from the finding of an elevated acidity and operation may be delayed.

CAUSES OF DEATH

Immediate postoperative death. Twenty-six patients did not live to leave the hospital. The primary and contributing causes of death in so far as could be determined are listed in Table VIII. The postoperative deaths in the entire group are 26 or 29.1 per cent. From 1927 to January 1, 1942, there were 46 cases, with an operative mortality of 41.3 per cent. In the following 3 years and 9 months almost as many operations were performed (43) as in the previous 15 years. In this latter period, that is from January 1, 1942, to October 1, 1945, the

TABLE VIII.—CAUSES OF DEATH FOLLOWING TOTAL GASTRECTOMY

Immediate postoperative deaths	
Abdominal conditions	
Peritonitis	14
Separation of suture line	5
Colitis	1
Subdiaphragmatic abscess	1
Ileus	1
Wound abscess	1
Pulmonary conditions	
Bronchopneumonia	8
Mediastinitis	4
Pulmonary infarction	2
Atelectasis	1
Tracheitis	1
Cardiovascular conditions	
Peripheral circulatory failure	4
Cardiac failure	3
Thrombosis of splenic artery and vein	1
Other conditions	
Parotitis	1
Total number of postoperative deaths	26
Specified— 24	
Unspecified— 2	
Subsequent deaths	
Metastases	30
Inanition	7
Intestinal obstruction	2
Stricture	1
Jejunocolic fistula with obstruction	1
Acute cardiac dilatation	1
Total subsequent deaths	43
Specified— 35	
Unknown— 8	

operative mortality was 16.3 per cent. This phenomenal decrease is the result primarily of four factors: (1) the increase in surgical skill arising from familiarity with the various techniques as well as the different problems encountered at operation, (2) better selection of cases, (3) the introduction of new bacteriostatic agents chiefly the sulfonamides and penicillin, and (4) better preoperative and postoperative care of the patient especially as to nutritional requirements and management of pulmonary and cardiovascular emergencies.

Subsequent deaths. Of the 63 patients who left the hospital, 43 were known to have died by March 1, 1946. The causes, which are known in 35 of these, are given in Table VIII. Recurrence developed in 85.7 per cent. This is interesting in view of the fact that the microscopic reports in these cases showed metastases in only 69.5 per cent. The discrepancy is probably more apparent than real.

TABLE IX.—SIGNS AND SYMPTOMS IN 57 PATIENTS FOLLOWING DISCHARGE FROM THE HOSPITAL

Dysphagia	16
Abdominal pain	14
Diarrhea	10
Nausea or vomiting or both	9
Failure to gain weight	7
Regurgitation	5
Fullness and abdominal distress	5
Weight loss	4
Heartburn	3
Weakness	3
Hypochromic anemia	3
Hiccup	3
Anorexia	2
Sore tongue	2
Anemia (unspecified)	2
Normochromic anemia	2
Intestinal obstruction	2
Other complaints	1 each

Sitophobia, burning in the throat, cough, cachexia, belching, mental depression, pleural effusion (without cancer cells), pernicious anemia salivation, and cheilitis.

SIGNS AND SYMPTOMS FOLLOWING DISCHARGE

The signs and symptoms occurring in 57 patients following discharge from the hospital are shown in Table IX. Dysphagia is the most frequent difficulty encountered in patients who have undergone total gastrectomy. In this series it was reported in 28 per cent of those who survived the operation. In the majority of cases this is caused by scar tissue at the site of the jejunoesophageal anastomosis and is easily remedied by dilatation. In some instances 1 or 2 dilatations suffice to control the situation, while in others 8 or more have been required at varying intervals. In some cases this symptom indicates a recurrence but dilatation should always be attempted. In 1 of our cases it is thought that the patient died prematurely because her local physician felt that since the symptom very probably indicated recurrence, dilatation was useless, with the result that the patient died of starvation.

Diarrhea was noted in 17 per cent. In several instances this symptom has been well controlled by adding hydrochloric acid to the diet. In others, bismuth subcarbonate powders have been equally successful. This complaint in our experience is usually short-lived and, as the jejunal pouch enlarges, gradually disappears.

Nausea and vomiting usually are early symptoms. The most frequent causes are nar-

TABLE X.—SURVIVAL CHANCE

Calculations based upon all patients who survived operation but have subsequently died (43 patients)

Less than 3 months	2
3 to 6 months inclusive	10
7 to 12 months inclusive	12
13 to 18 months inclusive	10
19 to 24 months inclusive	4
25 to 36 months inclusive	2
36 to 48 months inclusive	2
Over 48 months	1

Estimated chance of survival based upon 43 patients who survived operation but have subsequently died

50% have a chance of living 12 months
28% have a chance of living 18 months
16% have a chance of living 24 months
9% have a chance of living 36 months

Survival period of 14 patients who are still living

6 to 12 months inclusive	2
13 to 18 months inclusive	2
19 to 24 months inclusive	0
25 to 36 months inclusive	3
37 to 48 months inclusive	2
Over 48 months	5

Estimated chance of survival based upon 57 patients who survived operation, whether now living or dead

59.7% have a chance of living 12 months
38.6% have a chance of living 18 months
29.8% have a chance of living 24 months
21.1% have a chance of living 36 months

rowing at the anastomosis which may be the result of edema or spasm, or of the small initial capacity of the jejunal pouch. These symptoms yield frequently to antispasmodics and small and frequent feedings. The patient should be cautioned to eat slowly and to avoid any considerable amount of fluid with the meals. By systematically increasing the caloric intake over succeeding weeks, the capacity of the "new stomach" increases to a point at which three meals a day may be taken with comfort.

The failure to gain weight, which has been thought to be an almost inevitable sequela of total gastrectomy, has not been conspicuous in our series; it appeared in only 12 per cent. When recurrence is the cause, any relief will of necessity be temporary. From our experience, however, this difficulty may be avoided in a large number of cases by dilatation and careful postoperative dietary management.

Fullness and abdominal distress, like nausea and vomiting, are early symptoms and disappear with stabilization of the new physiologic processes.

In our series, insufficient blood studies were made postoperatively to generalize about the effect of the procedure except to state that a pernicious anemia-like picture was very rare.

SURVIVAL CHANCE

The most important factor in determining the validity of an operative procedure is the chance which it provides the patient for survival in contrast to his life expectancy without surgical intervention. The operative survival in this series has already been discussed. The determination of the survival chance of those individuals who do not succumb to the operation is complicated by the facts that many individuals were subjected to this surgical procedure at a time when it had not been entirely perfected and that others have undergone operation too recently to be of statistical significance. For this reason, the survival chance has been calculated in two ways: (1) based upon all the patients who have survived operation but have subsequently died, and (2) based upon all the patients who have survived operation whether now living or dead. The former calculations tend to give an underestimation of the probable present survival chance by virtue of the inclusion of operations performed during the early period. On the other hand, the latter possibly also tends to give an underestimation because a number of cases are included in which the operation has been performed at a recent date and also because there is no way of predicting with certainty the survival chance of individuals who are still alive.

Table X lists the life expectancy of patients who have survived the operation. It is apparent that at least 50 per cent of the patients will survive for 12 months, 28 to 38.6 per cent will survive 18 months, 16 to 29.8 per cent will live 24 months, and 9 to 21.1 per cent have a chance of living 3 years or more.

In our series 12 patients have survived for 3 years or more. Eleven of these had a total gastrectomy performed for a malignant lesion of which 1 was a leiomyosarcoma, 1 a malignant lymphoma, and 2 lymphosarcomas. Of these 11 patients with malignant lesions, 8 had regional metastases at the time of operation as evidenced by the finding of invasion of the regional lymph nodes removed at opera-

TABLE XI.—DATA ON 12 PATIENTS WHO SURVIVED 3 YEARS OR LONGER

Age and sex	Date of operation	End result		Metastasis	Diagnosis
		Dead	Living		
36 F	9-14-29	3½ years Carcinomatosis		Present	Carcinoma simplex
27 F	10-18-37		8 yrs. 5 mo. Well, 7 yrs.	Unknown	Leiomyosarcoma
50 M	11-29-38	4 yrs. 3 mo. Recurrence		Present	Adenocarcinoma
35 F	2-25-39		7 yrs. 1 mo. No recurrence Has pernicious anemia	Present	Lymphosarcoma
64 M	11-19-40		5 yrs. 4 mo. Feels fine	Present	Carcinoma simplex
51 F	5-10-41		4 yrs. 10 mo. Excellent Works hard	Present	Malignant lymphoma
60 F	11-14-41		4 yrs. Failing	Unknown	Unclassified carcinoma
02 F	1-24-41	3 yrs. Lung metastases		Unknown	Carcinoma
04 F	6- 4-42		3 yrs. 9 mo. Excellent	Absent	Carcinoma simplex
51 M	10-27-42		3 yrs. 5 mo. Excellent Works hard	Present	Lymphosarcoma
57 M	4-21-42	3 yrs. 8 mo. Well, 2 yrs. 8 mo. Carcinomatosis		Present	Carcinoma simplex
50 F	4- 1-43		3 yrs. Excellent Active	Absent	Chronic gastritis

tion. The longest survival was that of a 29 year old woman operated upon in 1937 for a leiomyosarcoma, who was living and well 8 years and 5 months after operation. Another patient, a 35 year old white woman, was operated upon in 1939 for a lymphosarcoma with involvement of the regional lymph nodes and was living 7 years and 1 month after operation. She has recently been examined at another hospital for a severe anemia, characteristic of pernicious anemia, and no evidence of recurrence was found. A third patient, a 64 year old white man with carcinoma simplex with microscopic metastases in the regional lymph nodes, was alive and in excellent health 5 years and 4 months after operation. A summary of all the patients surviving 3 years or more is given in Table XI.

POSTOPERATIVE NUTRITION

It is impossible to overemphasize the importance of nutritional care in the postoperative period of patients subjected to total gastrectomy. In many instances, if not in most, anorexia of varying duration has been a prominent symptom so that the patient is in negative nutritional balance at the time of operation. Consequently, his intake has not been sufficient to maintain his daily requirements nor to build reserve for the operative period. In addition, there may have been acute or chronic blood loss. Because operation must be performed as soon as the need for it is recognized, the nutritional care in the postoperative period must provide adequate resources with which to promote wound healing, ward off infection, and preserve new anatomical relationships which, in tissues lacking normal tone owing to undernutrition and toxic effects, are precarious.

In order to put the gastrointestinal tract as completely at rest as possible and so avoid stress at the suture lines, nothing is given by mouth for at least 3 days. During this period whole blood is given as indicated. If shock threatens or intervenes, plasma is given if

whole blood is not available or if hemoglobin and red blood counts show that whole blood is not required.

A total of 1500 cubic centimeters of 10 per cent glucose, with 1 or 2 ampules of soluble vitamin B complex and 500 milligrams of vitamin C, is given on the first day with 1000 cubic centimeters of a protein digest. Approximately 3000 to 4000 cubic centimeters of fluid is given in the first 24 hour period, depending on the patient's state of hydration. The difference between this requirement and the 2500 cubic centimeters already cited may be blood, plasma, or 10 per cent glucose.

The importance of limiting chlorides to actual requirements cannot be too frequently stressed. Although it is generally recognized that in the absence of vomiting, diarrhea, draining sinuses, or profuse diaphoresis, the average daily requirement of sodium chloride is 5 grams, patients all too frequently receive from 12 to 25 grams during the early postoperative period. Such therapy often leads to localized or generalized edema, wound disruption, and renal insufficiency.

With the recent advent of protein hydrolysates for parenteral administration, there has become available a valuable addition to the postoperative nutritional care especially of patients undergoing gastrointestinal surgical procedures. The routine postoperative use of such preparations is of great importance in the promotion of wound healing, resistance to infection, and prevention of edema. We advocate the administration of one of the available digests in amounts equivalent to at least 50 to 100 grams of protein daily until the patient is able to take adequate protein orally.

It is extremely important to maintain the caloric intake during the period in which the patient is fed parenterally. This is provided by the liberal use of 10 per cent glucose. A daily regimen of 1000 cubic centimeters of a protein digest in 5 per cent glucose and 2000 cubic centimeters of 10 per cent glucose with 500 cubic centimeters of normal saline solution provides 1200 calories, the approximate equivalent of 50 grams of protein and 8.5 grams of sodium chloride. This is continued until the patient has been transferred to an oral dietary regimen. Also, the patient is given parenteral vitamins as indicated previously.

On the fourth postoperative day 1 ounce of water is given by mouth every hour. On the following day 1 ounce of malted milk or gruel made with water is given hourly in addition to the water so that the patient takes something by mouth at half-hourly intervals. On the sixth and seventh days the amounts are increased by 1 ounce a day. On the eighth day a single feeding of soft solid food, such as soft egg, cereal, or custard, is added. On succeeding days small additional feedings of soft solid foods are given until the patient is eating 6 meals a day of a high protein, high carbohydrate, low fat, and low residue diet. If the amounts of this diet are increased by approximately 300 calories a week, the jejunal pouch adapts itself in many instances so that within 6 months the patient is able to maintain weight and strength with 3 meals a day.

SUMMARY

1. Eighty-nine cases of total gastrectomy, performed at the Lahey Clinic between 1927 and October 1, 1945, in patients ranging from 23 to 75 years of age, have been reviewed.

2. The postoperative mortality for the entire group is 29.1 per cent.

3. The postoperative mortality during the last 3 years and 9 months of the study during which 43 operations were done is 16.3 per cent.

4. Twelve patients have survived the operation for 3 years or more.

5. Calculation of life expectancy of patients surviving the operation shows that 50 per cent will survive 12 months or more; 28 to 38.6 per cent will survive 18 months; 16 to 29.8 per cent will live 24 months; and 9 to 21.1 per cent will live 3 years or more.

6. A plan for postoperative nutritional care is presented.

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COMPLETE FECAL DIVERSION ACHIEVED BY A SIMPLE LOOP COLOSTOMY

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DISSATISFACTION with currently employed methods of performing colostomy is implied in the numerous recent military publications (6, 7, 10) dealing with the problem of colostomy closure following the establishment of an external colic decompressive vent in the management of war wounds of the colon and rectum. The enthusiasm of some of my surgical colleagues, who have returned after several years of military service, over a method of achieving complete fecal diversion by the performance of a simple loop colostomy suggests that description of the technique is justified. This method of making a temporary colostomy has been in routine use at the University Hospitals for a period of 2 years. Moreover, incomplete division of a loop colostomy, with the posterior wall of the exteriorized segment used as the agent to divert the fecal stream, has been employed intermittently by the writer over a number of years, as it probably has by others. Recently, a patient returned to the clinic for whom such a colostomy was made by me 9 years previously. However, it is only within the past 2 years that I have become fully aware of the superiority of this simple means of accomplishing complete fecal deviation. In the abdominoanal "pull-through" operation for low-lying rectal cancers in which the rectal sphincters are spared, a complemental or supplemental colostomy occasionally is necessary (13, 14). That need of a procedure, which permitted temporary complete diversion of the fecal stream and which, at the same time, provided a stoma which was closed simply and easily, suggested the routine employment of the method herein to be described. In resection of the colon or rectum done at more than 8 centimeters from the anus, colostomy is unnecessary save for acute colic obstruction.

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HOW FECAL DIVERSION IS OBTAINED ORDINARILY

A loop colostomy is thought of ordinarily as a temporary external decompressive vent, which fails to provide complete fecal diversion. Grey Turner (1934) expresses well the sentiment of most surgeons on this particular when he says: "As a matter of fact, even for temporary colostomy it is better to divide the bowel completely, or fecal matter will be sure to reach the lower end. In actual practice, it is as easy to repair a complete colostomy as the sort of fecal fistula into which a partially divided bowel degenerates." Colonel Frank B. Berry (1946) recently stated that a loop colostomy should be completely divided after 7 to 10 days to achieve complete deviation of the fecal stream. He stressed the importance of exteriorizing the bowel adequately to prevent retraction, thereby insuring a satisfactory spur. Fallis (1946) follows this practice in performing colostomy for cancer of the left colon.

Even after complete division of the bowel, total fecal diversion ordinarily is not achieved completely because of the proximity of the two apertures. Hence the origin of the Devine "defunctionalizing" colostomy—a procedure which undoubtedly achieves satisfactory diversion, but which presents a problem of colostomy closure which is by no means simple. A number of surgeons have resolved the matter to their own satisfaction by making a "permanent type" of colostomy, placing the proximal and distal openings of the bowel at opposite ends of the wound; then, performing an oblique end-to-end anastomosis with excision of the colostomy at the time of closure. This latter plan meets the needs of the situation satisfactorily, but obviously constitutes a more formidable approach to the problem than the usual indication for the performance of a tem-

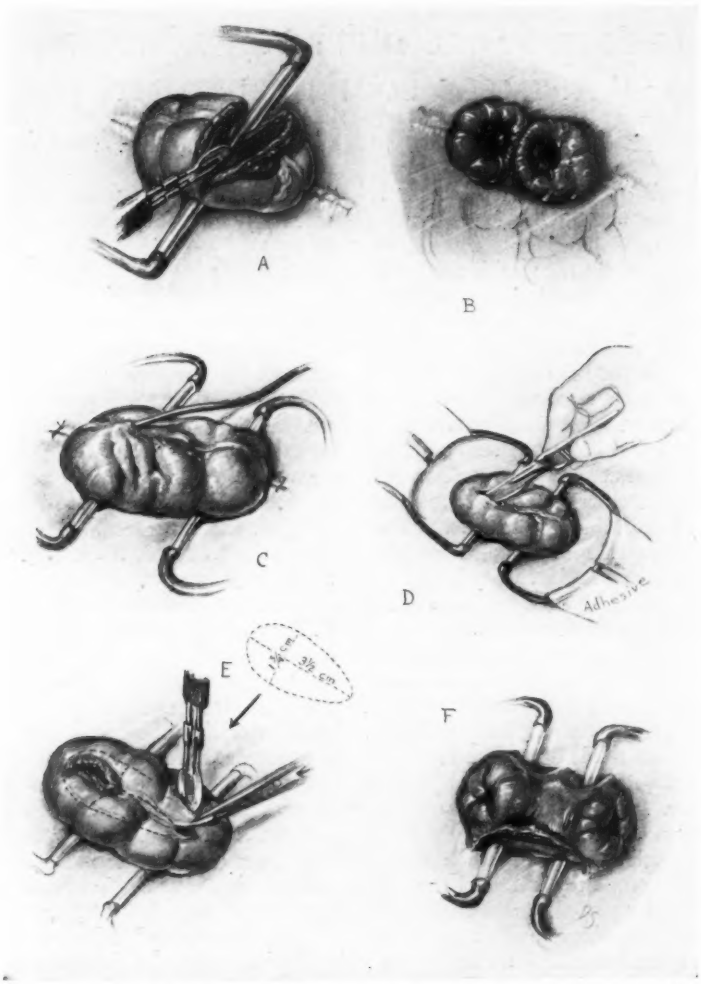


Fig. 1. Achieving complete fecal diversion with a loop colostomy (A to F—steps employed in making the loop colostomy). A, The conventional way of dividing the exteriorized loop transversely to achieve fecal diversion. B, The result after complete division; the lumens of the proximal and distal loops are separated only by the thickness of the walls of the two apposed loops. C, The technique described herein employing 2 glass rods and exteriorizing a somewhat more generous segment. A slit has already been made in the gut wall, proximal to the first glass rod. In the presence of acute obstruction and distention, a needle aspiration at this same site is performed on completion of operation and again in 6 hours, at which time a slit is made in the bowel wall with cautery (usually) or knife to permit the introduction of a catheter as is shown here. In the absence of obstruction, the exteriorized gut ordinarily is not opened until about 72 hours after operation, allowing the wound to become sealed more effectively. D, The adhesive fastening to the rubber tube engaged over the ends of the glass rods is shown. This maneuver insures adherence of the exteriorized loop throughout the length of the incision. E, Unroofing the proximal orifice by an elliptical incision; more of the roof overlying the proximal orifice is removed than the distal. F, Following excision of a portion of the anterior wall of the exteriorized segment, the mucosa everts and becomes adherent to the skin.

porary colostomy warrants. Madelung achieved complete diversion by dividing the colon and inverting the distal end. Kausch recommended placing an inflatable cuff in the distal segment

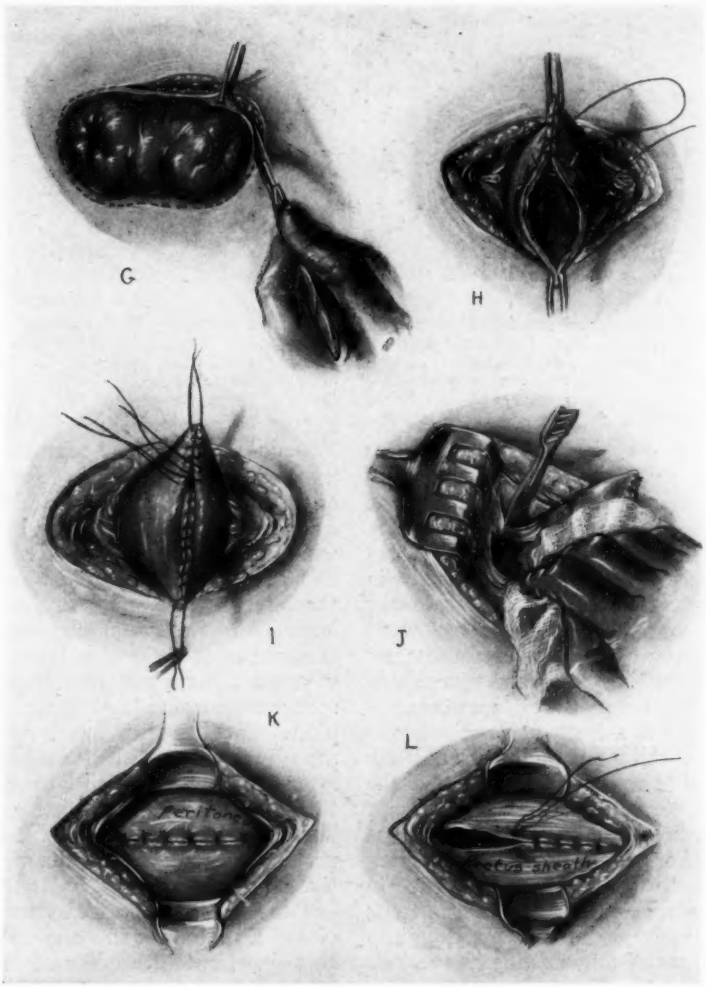
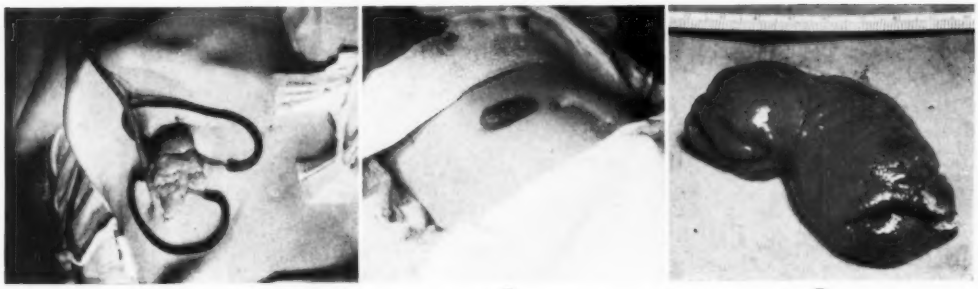


Fig. 1. (Continued—G to L—steps employed in closing the colostomy). G, It is obvious that the separation of the proximal and distal orifices of the exteriorized segment is far better than that achieved by the conventional method of dealing with the loop colostomy. An incision is made in the skin 2 to 3 millimeters from the mucosal edge. H, A running suture of fine catgut is employed to close the opened bowel transversely. I, The wound's edges are painted with a local antiseptic and the wound is redraped. After the gut is freed up adequately, a single row of interrupted fine silk sutures (No. 0000) is placed to invert the initial closure with catgut. J, The bowel is dissected completely free from the parietal peritoneum, permitting return of the bowel to the peritoneal cavity. This same procedure gives assurance that the peritoneum and posterior rectus sheath can be sutured satisfactorily. K, Suture of the posterior rectus sheath and peritoneum with interrupted sutures of silk (No. 000). L, Closure of the anterior rectus sheath (silk No. 000). After closure of the peritoneum (K), the wound is washed out with liberal quantities of saline solution and again after closure of the anterior rectus sheath (L).

a method with which the writer too has toyed, but without achieving complete diversion consistently. Baggio uses a pedicled strip of fascia, from the upper end of the wound, which he pulls through the mesentery and ties about the ascending colon in making a cecostomy.



A B C

Fig. 2. A, Photograph of an exteriorized transverse colostomy loop; a catheter has been placed in the proximal loop for decompressive purposes. B, Another similar loop colostomy after unroofing; note how effectively the colic orifices are separated. C, A sigmoid loop colostomy for the purpose of complete fecal diversion which was made by the writer in a patient 9 years ago (D. B., University Hospital No. 628722).

TECHNIQUE OF THE PROCEDURE

The making of the colostomy. Inasmuch as complete fecal diversion is achieved regularly when the method is performed properly, the colostomy may be employed as a temporary or even as a permanent measure. The usual temporary colostomy is made ordinarily in the right transverse colon, as was described for acute colic obstruction a number of years ago. For irremovable cancers of the rectum presenting obstruction, the same type of colostomy is performed on the sigmoid colon.

The technique of colostomy described previously (1936) is followed save in two particulars: (1) Two glass rods are drawn through the mesentery and placed beneath the exteriorized colon instead of one, the intent being to insure that the exteriorized segment of colon lies above skin level. (2) The colon is opened in the axis of the bowel and *not* transverse to its axis as is ordinarily done. Finally, the proximal orifice is unroofed by cutting away an elliptical portion of the anterior wall (Fig. 1E).

Following this maneuver, the two orifices of the bowel come to lie at opposite ends of the incision, separated by the posterior bowel wall. Care should be observed not to cut away too generous a portion of the anterior wall lest thereby the subsequent closure of the colostomy be made difficult. The margins of the opened bowel evert and become adherent to the skin edges. Maintenance of the two glass rods in position at opposite ends of the wound until it is healed precludes retraction of the orifices of the bowel. The usual circumstance is that shown in Figure 1G and Figure 2A. When the exteriorized segment of colon remains at skin level, the two orifices remain at opposite ends of the wound. It is partial *retraction* of the colostomy within the abdomen which causes the orifices to remain patulous and permit dumping from the proximal into the distal orifice. Similarly, employment of one glass rod in the middle of the exteriorized loop causes the orifices to become fixed in the wound at a lower level than is desirable in consequence of which fecal diversion is not complete. Patients with this type of colostomy are dismissed from the hospital 8 to 10 days after operation ordinarily, the general condition of the patient permitting, with one or both glass rods still in place. Both glass rods usually are removed by the 14th postoperative day.

The skin incision is made parallel to the axis of the transverse colon and directly over it. In the patient with acute obstruction of the colon, our practice is to tape a nickel over the umbilicus when the scout x-ray film is taken. This marker on the film serves as a landmark for the level of the incision. A transverse incision 10 to 12 centimeters in length directly over the right rectus muscle through all the layers of the abdominal wall permits even a distended colon to herniate out. Some surgeons have learned to their dismay that a distended transverse colon cannot be delivered through a vertical incision. When acute colic obstruction and distention are not present, a shorter skin incision will suffice. The two

glass rods are drawn through avascular areas in the mesentery. The omentum is freed from the loop to be exteriorized and dropped back into the abdomen. The parietal peritoneum and posterior rectus sheath are approximated to fatty tags at the margins of the bowel with a number of interrupted sutures of fine silk (No. 0000). No sutures are tied till all are placed. A smaller number of similar sutures are placed in the anterior rectus sheath approximating it to fatty tags at a higher level on the bowel. Finally, a few sutures are placed similarly in the skin. If the bowel is acutely obstructed and distended, a needle is inserted to measure intraluminal tension followed by aspiration. The exteriorized segment is covered with vaseline strips. In the presence of acute obstruction, the bowel is aspirated again in approximately 6 hours. In any case, every colostomy should be inspected for color and evidence of satisfactory viability 4 to 6 hours after completion of the operation. When obstruction is present, a catheter is inserted into a small hole made proximal to the most proximally placed glass rod. Complete diversion usually is achieved even at this stage. A linear incision 3 to 3.5 centimeters in length is made in the axis of the exteriorized bowel with a bedside cautery 3 or 4 days after operation. The unroofing of the proximal orifice may be done at the same time or a few days later. The details of the operation are shown in Figure 1. The usual measurements of the colostomy opening, when healing has occurred, are 5 centimeters in length and 3 centimeters in width. Two centimeters of bowel wall intervene between the adjacent margins of the proximal and distal orifices. When the ordinary loop colostomy is divided completely in a transverse direction, the two resultant orifices lie side by side. In patients with acute colic obstruction and distention, the ultimate measurements of the exteriorized segment obviously are greater.

Closure of the colostomy. The closure of such a colostomy is obviously simple. An incision is made in the skin adjacent to the bowel edges leaving a tiny rim of skin approximately 2 millimeters in width attached to the bowel. A running suture of catgut (No. 000) closes the bowel transversely. The wound is prepared again and the surgeon dons a new gown and gloves. The wound is enlarged and the peritoneal cavity is opened, care being observed to separate the bowel from the margins of the wound, all around and without injury to the bowel wall. A row of interrupted silk sutures placed over the catgut suture completes the closure.[1] The wound is then closed with two layers of interrupted fine silk suture (No. 000). After the peritoneum and posterior rectus sheath are closed, the wound is washed out with a generous quantity of saline solution and again after closure of the anterior rectus sheath.

In the making of the colostomy, as well as in its closure, the patient routinely has an indwelling duodenal tube to which suction is attached. When the colostomy is opened, the tube is withdrawn, and after closure of the colostomy, the nasal tube is withdrawn 48 to 72 hours after operation. The patient can be dismissed from the hospital ordinarily 5 or 6 days after operation. The writer does not consider succinylsulfathiazole or similar preparations a necessity for surgery of the colon. In primary reactions, if the anastomosis is made properly, such preparations are unnecessary as are also external diversionary decompressive vents. And, if the anastomosis is made improperly, all the drugs of the pharmacopeia usually will not rectify the situation. If in the closure of the colostomy any surgical house officer feels strongly upon the subject of the virtues of succinylsulfathiazole in mitigating the effects of surgery imperfectly performed, I am not averse to meeting his suggestion with an agreeable gesture. If he does not insist on it, this refinement is omitted. It is important to know that it is the satisfactory closure of a colostomy that makes return of the colon to the peritoneal cavity a safe procedure, a practice which this writer has followed routinely since 1929. A nice toilet of

[1]When the bowel is ready for final closure, the surgeon may snip out the temporary catgut suture. For 2 years, in making primary gastrointestinal anastomoses the writer has employed only a single row of interrupted silk sutures. Most of the surgeons in this clinic have adopted this technique as standard procedure in the making of anastomoses from the stomach to the rectum. A single row inversion made with interrupted sutures, without an inner row of continuous catgut assures wide and patulous orifices. Employment of a running stitch for the inner row causes puckering and consequent narrowing of the stomas.

the wound with the liberal use of generous quantities of saline solution makes it safe to effect primary wound closure with a reasonable assurance of the achievement of satisfactory healing.

SUMMARY

A simple loop colostomy may be employed to secure complete fecal diversion. Employment of 2 glass rods, drawn through the mesentery beneath the bowel and maintained in position until the wound is healed, fixes the exteriorized loop in the wound above skin level. The colon is opened by a slit in the axis of the bowel and the proximal orifice is unroofed by cutting away a small portion of the anterior wall. Such a colostomy is easy to make, as well as to close, and presents all the advantages of the more formal procedures in achieving complete fecal diversion.

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THE HYPERFUNCTIONING SINGLE ADENOMA OF THE THYROID

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IT is accepted that hyperfunction of an endocrine gland is associated with either a neoplastic or hyperplastic anatomic change. Neoplasia and hyperplasia, clearly differentiated by definition, have proved difficult to distinguish pathologically in disorders of the thyroid gland associated with hyperfunction. The debate as to whether the lesion of nodular goiter with hyperthyroidism is truly adenomatous or merely represents a late and lumpy stage of diffuse hyperplasia has long raged. The debate exists perhaps because there is no true difference between neoplasia and hyperplasia of the thyroid gland but more likely because the pathologist has lacked tools by which the differentiation can be made.

In disorders of certain other endocrine glands associated with overactivity, the problem of differentiating pathologically between neoplasia and hyperplasia is less confused. The division of the parathyroid system into four separate glands renders the gross recognition of the distribution of anatomic disease simpler than in the thyroid. The common type of anatomic change of the parathyroids encountered in hyperparathyroidism is that localized to but one of the four glands. The diseased tissue is then considered to be neoplastic and is called an adenoma. The distinct separation of the adrenal cortical gland into two parts offers a similar advantage.

The existence of a single adenoma of the thyroid causing hyperfunction, comparable to that found in patients with hyperparathyroidism, has been suggested (11), questioned (16), and not proved. Certain it is that the commonest type of anatomic disorder of the thyroid gland associated with hyperthyroidism, whether it be called hyperplasia, nodular or adenomatous goiter, diffusely involves the thyroid gland. So usual for the thyroid is this diffuse involvement that when a single adenoma is found in a patient with hyperthyroidism, one must be certain that smaller adenomas are not hidden elsewhere in the thyroid gland.

It might be of academic interest only to establish whether a single adenoma of the thyroid is ever associated with hyperthyroidism as it is in the parathyroid with hyperparathyroidism but its establishment should prove of practical value since it would offer a chance to learn about the functional capacity of adenomas and improve the judgment in therapy. With the advent of the two medical therapies, thiouracil (1) and radioactive iodine (2, 7), it is imperative to know not only whether the early relief of the hyperfunction of neoplasia is the same as of the hyperplastic type of the disease but more especially whether eventual malignant degeneration, about which apprehension is proper, will prove unequally evil in the two types.

Since the pathologist, using the conventional histologic methods, has not been able to tell us the degree of functional activity of the thyroid cell, we need criteria to establish the existence of a single adenoma of the thyroid with hyperfunction.[1] Clinically we should take for granted symptoms of hyperthyroidism and an elevated metabolic rate which are relieved by operative removal of the adenoma. There is in addition anatomic and biologic evidence which the surgeon can divulge and two laboratory tests which can be applied. The laboratory tests include inactivation of thyroid stimulating hormone of explanted thyroid tissue and radioactive iodine absorption by the thyroid gland.

[1]Certain special cytologic methods demonstrating the Golgi apparatus, mitochondria and secretory droplets have been introduced which are believed by many to indicate the functional activity of the thyroid cell. These methods require techniques which have proved not feasible in the routine pathologic laboratory.

From the Thyroid Clinic of the Massachusetts General Hospital.

TABLE I.—TEN PATIENTS WITH SINGLE ADENOMAS AND HYPERTHYROIDISM

Case number Year of operation	Sex Age	Duration of disease Preoperative	Eye signs	Metabolic Rate				Iodine effect	Wt. of adenoma gms.	Pathologist's diagnosis	Illustrations
				Initial	Preoperative	Postoperative 1–4 mos.	Postoperative Eventual				
1 1936	F 60	15 yrs.	Lid lag Stare	+60	+20	−12	− 5	?	31	Involution	Fig. 1 Chart 1
2 1940	M 48	4 yrs.	None	+51	+14	−20	−14	?	36	Hyperplasia involution	Figs. 2a and b Chart 2
3 1941	F 57	6+ yrs.	None	+60	+57	+ 1	− 6	0*	131	Involution	Figs. 3a and b Chart 3
4 1942	F 33	7 yrs.	None	+21	+27	−21	−14	0	19	Involution ?Hyperplasia	Fig. 4 Charts 4a and b
5 1945	F 47	9 yrs.	Lid lag	+37	+ 1	−16	− 6	?**	40	Hyperplastic adenoma	
6 1945	F 70	?18 mos.	None	+32	+32	Died at resection of gastric polyp		0	40	Struma nodosa micro et macro folliculare	
7 1945	F 61	18 mos.	Lid lag	+22	+ 7	No follow up		?	130	Hyperplasia—slight involution	
8 1945	F 65	6+ mos.	Lid lag	+ 1	−13	−16	−18	?	8	Hyperplasia involution	Charts 5 and 6 Diagram 4
9 1945	F 67	2 yrs.	Lid lag Stare ?Exoph.	+76	+51	+ 9	+ 5	0***	148	Involution hyperinvolution	
10 1946	F 48	5 yrs.	None	+24	+ 9	No follow up		?	20	Struma nodosa macro et micro folliculare	

*Patient also received X-ray treatment; there was no effect on the metabolic rate.
**Patient also received and did respond to thiouracil.
***Patient developed toxic reaction to thiouracil. Also received X-ray treatment without effect.

If an adenoma, involving only one portion of the thyroid apparatus, is hyperfunctioning and is the sole source of the hyperfunction then theoretically the remainder or uninvolved portion of the thyroid should not be normal but functionally resting and anatomically atrophic. Attention has already been called to the atrophy of the uninvolved parathyroids in hyperparathyroidism associated with an adenoma (3) and of the contralateral adrenal cortex in the patient with an adrenal cortical adenoma with hyperfunction. Such an atrophy of the thyroid gland has been shown to occur in animals which have been rendered thyrotoxic by large doses of thyroid extract and has been observed by us in one patient[1] who had taken large doses of thyroid extract and whose thyroid gland was exposed at operation under the mistaken diagnosis of Graves' disease. Such atrophy of a gland has been called an atrophy of disuse.

OBSERVATIONS

During the past 10 years 10 patients have been cared for in the Thyroid Clinic at the Massachusetts General Hospital whose thyroid glands fulfill the anatomic and biologic criteria of an hyperfunctioning single adenoma of the thyroid. Data regarding the nature of the disorder of these 10 patients are given in Table I. The patients were of varying ages; but one of the patients was male. All had symptoms and metabolic evidence of hyperthyroidism; a positive lid lag and stare were present in 5. In only one was there any suggestion of exophthalmos. The severity of the disease varied from crippling to a mild disability.

[1]The 40 year old dietitian of a woman's college was cared for at this hospital in 1935 because of increasing nervousness. She reported that she had been concerned about her obesity and some months previously had succeeded in losing weight by stringent dieting. Examination disclosed findings typical of exophthalmic goiter of moderate severity except for the absence of a palpable goiter. She had bright starey eyes with a positive lid lag, fine tremor, rapid pulse and widened pulse pressure. Her basal metabolic rate was +62. In spite of the absence of a palpable goiter, a diagnosis of Graves' disease was made, believing it to have been induced by a too rapid loss of weight. It was believed that the goiter was hidden behind the manubrium. She was placed on potassium iodide to which she apparently made a prompt response, her basal metabolic rate reaching +14 in 17 days. At operation she proved not to have a goiter but on the contrary, a small, soft avascular thyroid consistent with atrophy. The pieces of each lateral lobe removed for diagnosis were reported as "involution" by the pathologist. Confronted with this anatomic information, postoperatively the patient admitted, although she had denied this fact preoperatively, to having taken for some months previously large doses of dessicated thyroid to which she had access in the college infirmary.

CASE 4. (See Fig. 4 and Charts 4a and b.) A 33 year old woman was admitted to the hospital complaining of a gradually enlarging goiter of 7 years' duration. Although the patient had no difficulty in swallowing she was constantly aware of a sensation of pressure in the neck. During the months immediately prior to admission she had noticed slight trembling of her hands and pounding of her heart when she lay on her left side at night. Hungry all the time, she had gradually been gaining weight for several months. She had not experienced nervous irritability, heat intolerance, dyspnea, or change in bowel habit.

On examination, the patient displayed a slight tremor of the extended fingers. The hands were warm but not excessively moist. There were no eye signs. A firm, nontender, rounded nodule, 5 centimeters in diameter was palpable in the upper portion of the left thyroid lobe. The isthmus and right lobe of the thyroid could not be felt. Basal metabolic rates of plus 19, 21, and 24 were obtained. A diagnosis of thyrotoxicosis, probably due to a hyperfunctioning adenoma, was made. Saturated solution of potassium iodide, 5 drops twice daily, was prescribed and the patient discharged home to be readmitted for operation.

When readmitted 2 weeks later, she stated that the only symptomatic change was a decrease in the sensation of pressure in the neck. Her weight had remained stationary. At operation, the left lobe of

Fig. 1. The hyperfunctioning adenoma and atrophic uninvolved thyroid tissue in Case 1. The encapsulated adenoma is considered to have been the source of the excessive hormone production because the uninvolved tissue was grossly and evenly atrophic. There was a bit of the uninvolved thyroid tissue at both upper and lower poles of the adenoma, all that remained of the right thyroid lobe. The separate, shrivelled piece of tissue represents the entire isthmus and anterior half of the left thyroid lobe. (For the effect of the adenoma on metabolic rate, see Chart 1.)

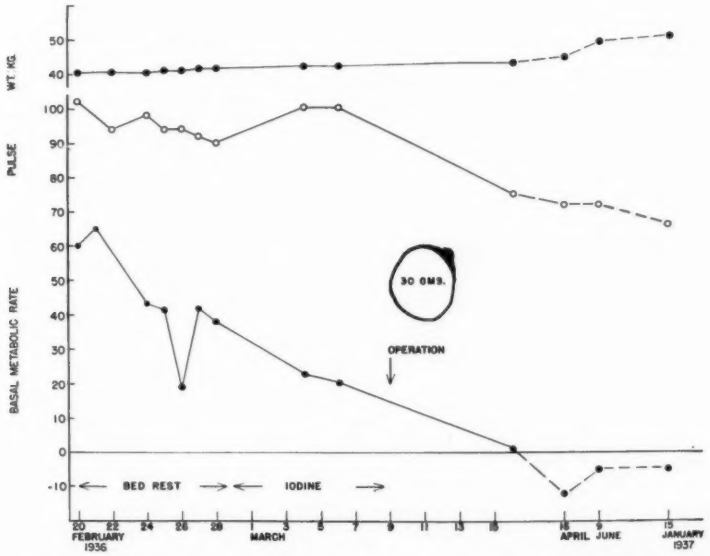

Chart 1. The effect on metabolic and pulse rates and weight of extirpation of the single adenoma of Case 1 (Fig. 1). Bed rest, but probably not iodine, was followed by partial subsidence of the thyrotoxicosis immediately before the operation. The depressed metabolic rate found soon after operation proved to be transient.

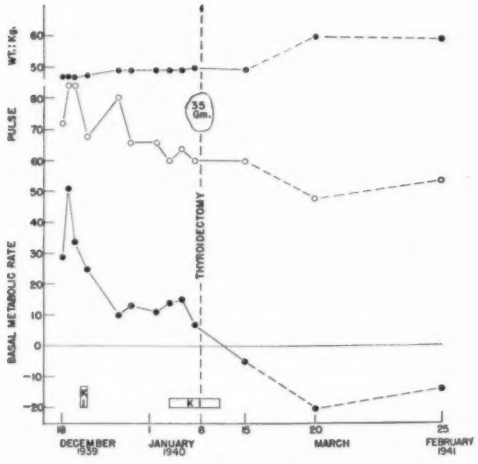

Chart 2. The effect on metabolic and pulse rates and weight of excision of the single adenoma of Case 2 (Figs. 2a and b). It is possible that iodine and bed rest together induced the partial remission of the hyperthyroidism prior to operation.

the thyroid was found to consist largely of a solid tumor measuring 5 by 4 by 3 centimeters. At the posterior portion of both the upper and lower poles, there was a small mass of uninvolved, atrophic tissue. There was also a rim of atrophic thyroid on the medial side of the adenoma and on the anterior surface of the trachea. The isthmic tissue was so thin as to be hardly recognizable. The right lobe was also atrophic, measuring 3 by 2 by 1 centimeter. Microscopically the adenoma showed hyperplasia and involution. Biopsies of the uninvolved tissue on the left side and of the right lobe were consistent with involution.

Postoperatively, the patient was less restless than before and no longer conscious of the beating of her heart. Her appetite was less voracious but her weight remained stationary. The basal metabolic rate 6 weeks after operation was minus 21; four months later, minus 14.

In Table II for comparison with the patients having single adenomas and hyperthyroidism are given the data on one patient with a large adenoma and two small satellite adenomas associated with hyperthyroidism, and three patients with single adenomas but no hyperthyroidism. These latter three have been selected from a group of 15 patients with single nodules and no hyperthyroidism in whom radioactive iodine studies have been carried out.

Gross anatomy. At operation on the 10 patients with single adenomas and hyperfunction the anatomic lesion was found to be circumscribed. In 8 patients the lesion was confined within a clearcut capsule, involving only one part of a lateral lobe as in Cases 1 and 2 (Fig. 1 and 2b). In the other 2 patients, Cases 3 and 9, (both elderly and with longstanding disease), the lesion involved the entire lateral lobe, there being no uninvolved tissue recognizable on that side (Fig. 3b). In all 10 patients the uninvolved tissue was grossly consistent with atrophy. The uninvolved residual of the lateral lobe of the 8 cases, and the isthmus and the contralateral thyroid lobe of all 10, were smaller than the expected normal, and in some cases were shrivelled (Fig. 1 and 2b). In all cases the uninvolved tissue varied from the normal; it was softer and more pliable, the surface convolutions were less prominent or absent, the color was a little paler and speckled with white, the vessels were less prominent, and on cut sections the tissue was judged to be less

TABLE II—FOUR PATIENTS WITH FINDINGS IN CONTRAST TO THE TEN PATIENTS IN TABLE I

Control Case number Year of operation	Sex Age	Duration of disease Preoperative	Eye signs	Metabolic rate				Iodine effect	Wt. of adenoma gms.	Pathologist's diagnosis	Illustrations
				Initial	Preoperative	Postoperative 1—4 mos.	Eventual				
1C 1942	F 23	18 mos.	lid lag	+56	+12	+14	+ 2	+	35	Involution	
2C 1945	F 52	1 yr.	None	0	— 8				45	Involution Hyperinvolution	Chart 5, diagram 3 Chart 6, diagram 3
3C 1945	M 53	30 yrs.	None	— 1		— 4			55	Involution Hyperinvolution	Chart 6, diagram 3A
4C 1945	F 28	15 mos.	None						17	Involution Hyperinvolution	Chart 6, diagram 3B

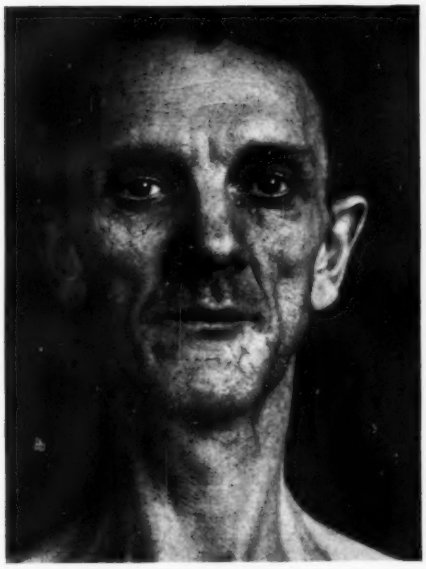

Fig. 2a. Case 2. There is no exophthalmos or stare. Loss of weight is apparent. The splaying of the lower end of the right sternomastoid muscle by the adenoma in the left lobe of the thyroid is visible. (The thyroid adenoma removed and its effect on the metabolic rate are shown in Figure 2b and Chart 2.)

vascular. So soft was the gland in 1 or 2 cases that the thyroid and cricoid cartilage could be felt through the thyroid tissue. In no instance was a second nodule seen or felt at operation. . In the 4 control patients the anatomic findings at operation differed significantly. The first patient whose data are summarized in Table 11, Case 1C, was believed preoperatively to be one whose hyperthyroidism was due to a single adenoma. The hyperthyroidism was definite and but one nodule was palpable on physical examination in the region of the thyroid gland. At operation the uninvolved tissue, however, was not atrophic. The isthmus and lobe contralateral to that containing the preoperatively palpable nodule were fully as large, firm and vascular as normal and further scrutiny disclosed two small nodules in the posterior position of the contralateral lobe. The large nodule was excised *in toto* and a small portion only of the contralateral lobe was taken for microscopic section and thyroid stimulating hormone inactivation study.

Fig. 2b. The hyperfunctioning adenoma and rim of atrophic uninvolved tissue of Case 2. The adenoma was encapsulated, firm, fleshy and brown while the uninvolved thyroid tissue was soft, diffusely shrivelled, and avascular. The adenoma is considered to have been the source of the excessive hormone production because of the gross atrophy of the uninvolved portions of the thyroid gland and because its removal resulted in relief of the hyperthyroidism. (See also Fig. 2a and Chart 2.)

CASE 1C. A 23 year old woman was admitted to the hospital complaining chiefly of nervousness of 12 months' duration. She had been well until about one year prior to admission when without obvious cause she became irritable and easily upset. Six months before admission she first noticed a swelling in her neck which slowly increased in size. Three months prior to entry she began to experience palpitation, exertional dyspnea, increased frequency of bowel movements and excessive perspiration. She felt increasingly fatigued and gave up bowling, swimming and dancing. Her weight remained stationary despite a noticeably increased appetite.

On examination she appeared warm, sweaty, and flushed. There was a slight tremor of the extended fingers. No eye signs could be elicited. The left lobe of the thyroid was replaced by a soft nodule measuring 5 by 7 centimeters, which displaced the trachea to the right and extended down to the sternal notch. A small amount of tissue was palpable to the right of the trachea in the thyroid region. The pulse was 110 and bounding in character. Basal metabolic rates of plus 28, 24, and 30 were obtained. A diagnosis of thyrotoxicosis, possibly due to a hyperfunctioning adenoma, was made. After 2 weeks of therapy with potassium iodide, 15 drops a day, the basal metabolic rate had fallen to minus 6 and the patient's weight had increased 2.5 kilograms. She was discharged home on iodine therapy, to be followed in the out-patient clinic.

Five months later she was readmitted for excision of the nodule because of its increase in size. She had taken the iodine faithfully and felt less nervous. Her retmor and frequent bowel movements continued

Fig. 3a. Case 3. The calm expression belies the presence of hyperthyroidism. The unilateral goiter subsequently removed is shown in Figure 3b and its effect on the metabolic rate in Chart 3.

and her weight remained approximately stationary. The physical findings were essentially unchanged except that the nodule in the left lobe of the thyroid seemed larger, measuring 7 by 7 centimeters. Basal metabolic rates of plus 46, 43 and 35 were obtained. After a month's bed rest, the rate had fallen to plus 12. At operation, the left lobe was found to contain a large nodule and the otherwise normal appearing right lobe to contain two small nodules. The nodule in the left lobe was resected in entirety, leaving about 4 grams of uninvolved, apparently normal tissue. A biopsy specimen was taken of the uninvolved normal appearing tissue of the right lobe. Microscopically, all sections of the left lobe nodule showed involution. The tissue removed from the right lobe was consistent with normal.

Postoperatively, the patient gained 5 kilograms in weight and was entirely relieved of her symptoms. The basal metabolic rate 10 days after operation was minus 10.

The remaining 3 control patients of Table II whose thyroid function is considered to have been within normal limits were each found at operation to have a single adenoma. The uninvolved tissue was considered to be consistent with normal but in the last, Case 4C, the note was made at operation that the uninvolved parts of the gland were on the small side of normal and unusually soft; partial atrophy was considered possible. The results of the radioactive iodine determinations in this case were therefore not surprising (see below under "Radioactive Iodine Uptake").

Fig. 3b. The left sided goiter and biopsy specimen of the atrophic right thyroid lobe of Case 3. The entire left lobe of the gland was involved in the anatomic disorder but on section the disorder proved to be uneven. In the upper half was a smooth nodule, the tissue of which is comparable to the homogeneous adenomas illustrated in Figures 1, 2b, and 4. The remainder of the goiter was made up of irregular whorls of cellular thyroid tissue; the septa were indefinite. The entire isthmus and right thyroid lobe were atrophic. A similar, irregular, and unilateral goiter, with atrophic uninvolved tissue elsewhere, was encountered in Case 9. The adenomas of the 8 other cases were of the homogeneous type. (See also Fig. 3a and Chart 3.)

Microscopic anatomy. The tumors of all 14 cases, that is including the control cases, were variously classified and without any correlation with function by our pathologists as involutional nodules, involution and hyperplasia, hyperplastic adenoma and struma nodosa micro et macro folliculare. The biopsy of the uninvolved tissue was described as either normal or involution, there being no correlation with the gross finding of atrophy.

Operative relief. All 10 of the patients with single adenomas and hyperfunction were relieved of the thyrotoxicosis by operation. Operation in each case consisted of total excision of the adenoma and resection of a certain amount of the atrophic uninvolved tissue. In the first 2 cases, the isthmus and approximately half of the contralateral lobe were resected (Fig. 1 and 2b); in the others only a small portion of the atrophic tissue was removed as a biopsy (Fig. 3b and 4).

There was a transient drop in metabolic rate to subnormal levels immediately following operation in 3 of the 7 patients in whom an adequate number of determinations were made (Charts 1, 2, and 4a). In a fourth, Case 8, the

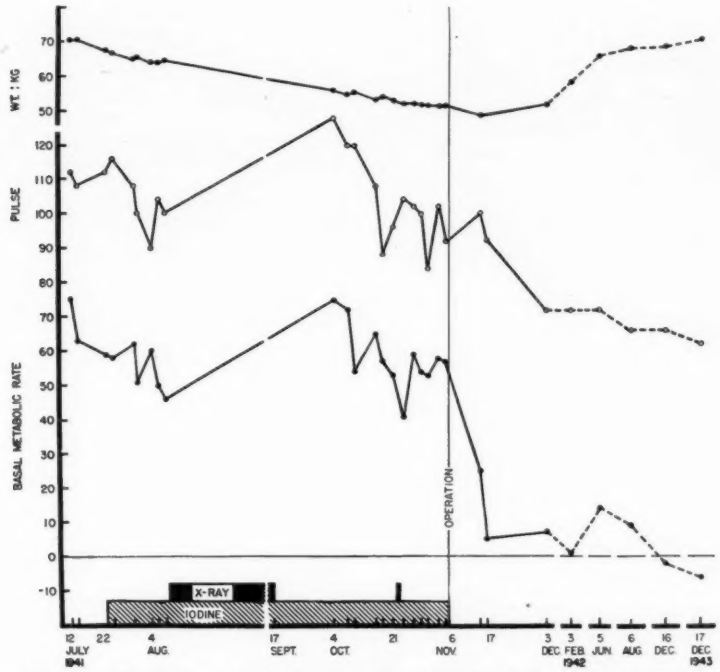

Chart 3. The effect on metabolic and pulse rates and weight of extirpation of the unilateral goiter of Case 3 (Figs. 3a and b). Both iodine and roentgen irradiation failed to induce a remission of the thyrotoxicosis.

metabolic rate remained subnormal but there were no signs or symptoms of hypothyroidism.

The transient period of hypometabolism following operation suggests that there may have been functional inactivity of the uninvolved tissue. Permissible in Cases 1 and 2 in whom the more radical resection was done, the fall should not have occurred in the other if the uninvolved tissue was normal physiologically. Removal of one of two normal lateral thyroid lobes at parathyroid exploration, which had been carried out in several of our hyperparathyroidism cases, has not been followed by any such decrease in thyroid function. The ultimate return of the metabolic rate suggests capacity of the uninvolved tissue to recover and retain normal function. This is in support of the view that such atrophic tissue is not diseased but suffers only from disorder of function.

Thyroid stimulating hormone inactivation. The adenomatous and uninvolved atrophic tissues of 2 patients with single adenomas and hyperthyroidism (Cases 4 and 7) and of the one patient with multiple adenomas with hyperthyroidism (Case 1C) have been studied for their ability when explanted to inactivate the thyroid stimulating hormone of the anterior pituitary gland. This action has been used as a test by Rawson, Graham, and Riddell to differentiate between normal and various pathologic human thyroid tissues (13, 14). A slice of thyroid tissue, weighing approximately 150 milligrams is incubated for 24 hours in a substrate containing 7.5 units of thyroid stimulating hormone (Junkman and Schoeller guinea pig units). Upon removal of the thyroid tissue the residual activity of thyroid stimulating hormone is measured by the effect of the substrate upon the mean cell height of the thyroid gland of the injected baby chick.

It has been found that an explant of normal human thyroid tissue inactivates 3.5 units (14) (Chart 5, diagram 1). (The normal thyroid

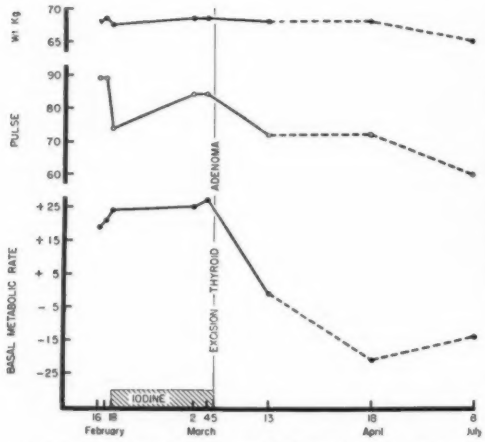

Chart 4a. The effect on metabolic and pulse rates and weight of removal of the single adenoma of Case 4 (Fig. 4 and Chart 4b). Iodine failed to produce a remission of the thyrotoxicosis.

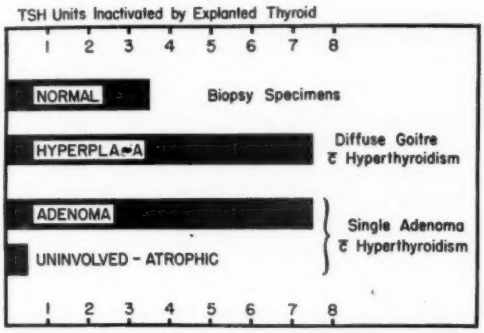

Chart 4b. Inactivation of thyroid stimulating hormone by explanted thyroid tissue. The thyroid tissues tested were: (1) normal being pieces of glands removed at parathyroid exploration from 7 patients with normal metabolic rates; (2) hyperfunctioning hyperplastic, consisting of portions of diffuse goiter resected for hyperthyroidism in 20 patients prepared for operation with iodine; (3) hyperfunctioning adenomatous and (4) its associated grossly atrophic uninvolved tissue from Case 4. The patient was relieved of the hyperthyroidism by resection of the adenoma and biopsy only of the uninvolved tissue. (See also Fig. 4 and Chart 4a.) The patient received iodine before operation. Explants were sliced and trimmed to weigh approximately 150 milligrams. Beef antuitrin-T was used.

tissue was removed from 7 patients undergoing parathyroid exploration for hyperparathyroidism.) The portions of diffuse hyperplasia resected from 20 patients with hyperthyroidism who were prepared for operation with iodine inactivated all of the thyroid stimulating hormone present in the bathing fluid (Chart 5, diagram 2).

A portion of the adenoma removed from Case 4 (patient with a single adenoma and hyperthyroidism) was found to inactivate all of the thyroid stimulating hormone (Chart 5, diagram 3). The piece of the uninvolved atrophic thyroid tissue resected from the same patient was found to inactivate none of the hormone (Chart 5, diagram 4). Similar findings were obtained in the tissues removed from Case 7.

The failure of the grossly atrophic, uninvolved tissue found in the presence of a single adenoma in the patients with hyperthyroidism to inactivate thyroid stimulating hormone suggests that there has been a prolonged absence of the stimulus to produce thyroid hormone. The site of inhibition of anterior pituitary stimulation of the thyroid gland by an excess of thyroid hormone has been discussed elsewhere (15).

The results on the tissues resected from the patient with the multiple adenomas with hyperthyroidism (Case 1C) showed complete inactivation by the large adenoma but only normal inactivation by the nonadenomatous tissue from the contralateral thyroid lobe. This lobe was not grossly atrophic. The finding of normal inactivation by the grossly normal tissue of a patient with active hyperthyroidism indicates either that all normal tissue is not put at physiologic rest and therefore does not undergo atrophy in the presence of an hyperfunctioning adenoma or that what was grossly compatible with and believed to be normal tissue in this patient was really diseased. The presence of the two small satellite adenomas in the contralateral lobe is in favor of the latter.

Radioactive iodine uptake. The second laboratory method of judging objectively the physiologic or secretory activity of thyroid tissue is the measurement of the amount of uptake of radioactive iodine (4, 5, 6). As might be anticipated the amount of the radioactive isotope absorbed in the thyroid is proportional to the secretory activity of the gland. It has been found that the thyroid gland of a normal person given a small or tracer dose of radioactive iodine will absorb approximately 40 per cent

of this iodine in the first hours and that the other 60 per cent will appear in the urine within 48 hours. It has also been established that the avidity for iodine is increased in the hyperplastic thyroid of a patient with exophthalmic goiter.[1] In such hyperplasia associated with increased activity 80 to 90 per cent of the administered iodine is collected in the thyroid substance and only 10 to 20 per cent is excreted in the urine in the first 48 hours. In contrast, in a patient with a hyperplastic goiter and hyperthyroidism under treatment with thiouracil, the absorption of iodine is partially blocked. Less than 20 per cent of the radioactive iodine injected is held by the thyroid while more than 80 per cent passes out through the kidney in the first 48 hours (17). The initial observations of such iodine absorption by the thyroid, determined by Geiger counter scrutiny of the neck and measurements of the actual urinary excretion, have been checked recently by direct measurement of the radioactive iodine content of thyroid tissue surgically removed as a biopsy (8, 10, 17).

The radioactive iodine absorption by thyroid tissue has been measured in one patient with a single adenoma and hyperthyroidism (Case 8) and in 15 patients with single nodules without thyrotoxicosis. The radioiodine content of both the tumor and uninvolved tissues has been measured. The radioactive iodine has been given to the patient by mouth 1 to 7 days before operative extirpation of the glandular tissue. The adenoma of the case with hyperthyroidism showed an avidity for iodine comparable to that found in untreated hyperplastic goiter with hyperthyroidism, while the uninvolved, grossly atrophic tissue failed to take up any measurable quantity of radioactive iodine (Chart 5, diagram 4 and Chart 6, diagram 4). These findings strongly suggest, indeed on present knowledge indicate, that the entire output of hormone was from the adenoma and that the adenoma, therefore, must have been responsible for the thyrotoxicosis.

Study of the 15 adenomas not associated with hyperthyroidism indicates that adenomatous tissue varies in its functional activity.

[1]The tracer dose of iodine contains approximately 50 micrograms of iodine, an amount known to be too small to influence the function of the gland. This amount is a small portion of the daily exchange of iodine and an even smaller proportion of the content of iodine of the gland.

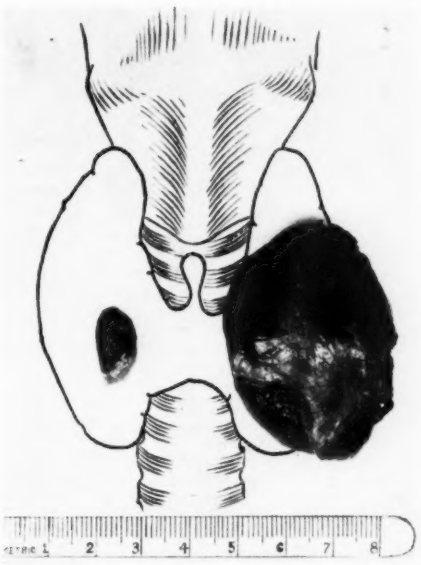

Fig. 4. The hyperfunctioning adenoma of the left thyroid lobe and biopsy specimen from the atrophic right lobe of Case 4. The adenoma was sectioned, a piece removed from the anterior half, and then the halves were replaced. The exposed cut surface of the posterior half shows the adenoma to be of the homogeneous cellular type with a single clearly demarcated capsule. There is a small remnant of shrivelled, uninvolved thyroid tissue on the lateral surface of the adenoma. The effect on metabolic rate of its removal, the inactivation of thyroid stimulating hormone by it and the atrophic uninvolved tissue are shown in Charts 4a and b.

Three examples have been chosen from the 15 patients to illustrate the distribution in activity and are shown together with the case with hyperthyroidism in Chart 6. In the first, labelled 3, the uptake of radioactive iodine, and therefore the hormonal secretory activity, is minimal while that of the uninvolved tissue is normal. The ratio of the uptake of uninvolved to adenoma is 23:1. In the second case with normal hormonal output, the ratio of uptake of the uninvolved to adenoma is but 7:1. The avidity of the uninvolved is near the minimal amount expected of normal tissue. The activity of the adenoma is still below that of normal tissue. This case is labelled 3A. The diagram labelled 3B depicts a reversal of the ratio of uptake of iodine in a patient with overall normal thyroid activity. In this case the uptake of iodine per gram of thyroid tissue was considerably more in the adenoma than in

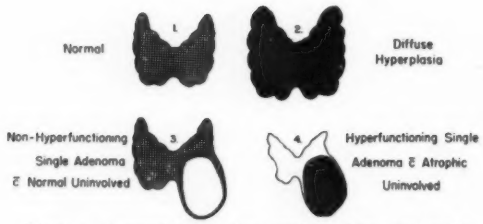

Chart 5. Proportionate size, configuration, and radioactive iodine uptake of normal and diseased thyroid glands. The intensity of the shading indicates the avidity of the tissue for a tracer dose of iodine. Diagram 1 represents a normal gland. Diagram 2 is that of a patient with diffuse hyperplasia with hyperfunction (Graves' disease); it is therefore drawn diffusely larger than the normal and colored blacker because of an increased avidity for iodine. Diagram 3 represents a single adenoma with but little iodine uptake in a patient with normal thyroid function; the uninvolved gland is normal in size and iodine uptake (Case 2C, see also Chart 6, diagram 3). Diagram 4 represents the findings in Case 8 with a single hyperfunctioning adenoma. The adenoma absorbs an increased amount of iodine while the uninvolved takes up none. The uninvolved tissue is atrophic and shrunken. (See also Chart 6, diagram 4).

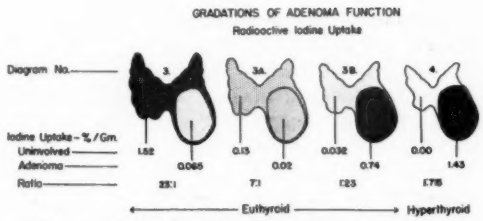

Chart 6. Gradations of function of thyroid adenomas indicated by their absorption of a tracer dose of radioactive iodine. The intensity of the shading is proportionate to the avidity of the tissue for the iodine. The measured iodine uptake of each tissue is given below the diagram; the figures represent the per cent of the dose of iodine found per gram of tissue. The ratio of iodine uptake of uninvolved tissue to adenoma is given in the lowest line of figures. In the first three diagrams (3, 3A, and 3B) the overall thyroid function was normal yet the activities of the adenoma and uninvolved tissues differed. In diagram 3 are given the findings in Case 2C (see also Chart 5, diagram 3), in diagram 3A those of Case 3C, and in diagram 3B those of Case 4C. With increasing adenoma function there is a decrease in the function of the uninvolved tissue with overall decrease in size or partial atrophy in diagram 3B as compared with diagram 3. Diagram 4 represents the finding in Case 8 (see also Chart 5, diagram 4) with a hyperfunctioning adenoma; there was no uptake of iodine by the atrophic uninvolved tissue.

the uninvolved tissue. The ratio of uninvolved to adenoma was 1:23. This finding, coupled with the gross appearance of the uninvolved tissue, which was consistent with partial atrophy, suggests that the adenoma was secreting the large part of the hormone requirements of the patient and that the uninvolved tissue was at partial rest. The findings in these 3 cases are to be contrasted with diagram 4 which depicts the patient with hyperthyroidism. (Diagrams 4 of Charts 5 and 6 are of the same patient.) In this case the given ratio of 1:715 is arbitrarily set by the sensitivity of the method since there was no measurable radioactivity in the uninvolved tissue.

Comparison of these 4 cases suggests, first, that secretory activity of an adenoma is not all or none but that there are many gradations; second, that if the secretory activity of the adenoma is high and the size of the adenoma sufficient, hyperthyroidism results; and third, that such hyperthyroidism is accompanied by depression of the activity of the uninvolved gland.

Responses to iodine, thiouracil, and irradiation. It is not clear that the hyperthyroidism of any of the patients was alleviated as a result of the administration of iodine. The metabolic rate fell in 6 patients following iodine but it is possible that the fall was the result of continued bed rest or other cause (Charts 1 and 2). Certain it is that there was no response in the other four (Chart 4a).

The adenomas of 2 patients, Cases 3 and 9, were exposed to roentgen irradiation before operation. In neither case was this treatment followed by any change in the metabolic rate.

Only one of the 10 patients was treated with thiouracil, Case 5; neither the inactivation of thyroid stimulating hormone nor radioiodine absorption was measured in this patient's gland. The thiouracil was accompanied by a drop of 23 per cent of the metabolic rate in 14 days. A response to thiouracil is to be anticipated; part of the fall in this patient may have been due to rest. The patient at a previous hospital admission had made an apparent response to iodine which had then been omitted for some months prior to the thiouracil treatment.

FURTHER COMMENT

The gross anatomic findings and the tests of function, inactivation of thyroid stimulating hormone, and collection of radioactive iodine, have delineated the single adenoma with hyperfunction as a disease entity of the thy-

roid gland. Not only does the adenoma inactivate an excess of the anterior pituitary hormone but it has been shown to be the only part of the thyroid gland which absorbs iodine. Since iodine is a chemical requisite of the thyroid hormone, the adenoma is the only part forming hormone and must therefore be responsible for the excess. The uninvolved tissue which collects no iodine and inactivates no pituitary stimulating hormone is apparently at physiologic rest and is anatomically atrophied. Thus, the term adenoma, used to denote a benign neoplasm, has been given a physiologic as well as anatomic meaning. Strictly, neoplasia means an abnormal growth of tissue which takes place without regard to the laws governing the normal portions of the gland. In these cases the excessive function has been assumed by the adenoma indicating a disordered secretory activity in addition to the pathologic cell growth. In contrast the uninvolved tissue obeys physiologic laws and rests in the presence of an excess of the hormone; its disorder of function is secondary and the tissue is not in itself diseased.

The single adenoma is a rare cause of hyperthyroidism. It is best considered as a pathologic type at the extreme from the diffuse hyperplasia which is the common type associated with hyperfunction. The disease types in the thyroid and parathyroid glands are thus reversed.[1] As with hyperparathyroidism due to adenoma, hyperthyroidism may also be associated with more than one adenoma. We have encountered 2 cases with two adenomas each. That the neoplasms, or adenomas, were the cause of the hyperfunction is indicated by the accompanying atrophy of the uninvolved tissue comparable to that found in the cases with the single hyperfunctioning adenomas described in this paper. Doubtless cases will be found in which there are multiple adenomas, all hyperfunctioning. The differentiation of the lumps as true neoplasms will depend upon the demonstration of physiologic rest of the uninvolved tissue in contrast to hyperfunctioning paranodular tissue of nodular goiter with hyperthyroidism (12). Indeed henceforth distinction between lumpy diffuse goiter with hyperthyroidism and true neoplastic or adenomatous goiter must be made by simultaneous scrutiny of all the nodules and the uninvolved or paranodular tissue.

The observation that the disease process in the thyroid is localized to one part of the gland suggests that the origin of the disease is different from that of the diffuse hyperplasia type in which all of the tissue is acting beyond normal physiologic control. Our studies give no clue as to the nature of the initiating process. It is of interest that the clinical disease produced by the hyperfunctioning single adenoma did not differ significantly from Graves' disease with the diffuse goiter. There is a suggestion that eye signs, particularly exophthalmos, were less frequently encountered but the number of cases is too small to be sure that this difference was not due to the age of the patients. That the function of the majority of the adenomas was not affected by iodine is certain.

Of significance to the surgeon is the finding that the uninvolved tissue obeys physiologically the law of supply and demand as far as function is concerned and is therefore not diseased. Nothing is to be gained by excising it. Indeed it would be better to leave all of it behind, the better to insure more prompt and complete return of function. If the surgeon is familiar with tissue atrophied by disuse, little difficulty will be encountered in recognizing it.

We have not had an opportunity to test the efficacy of radioactive iodine in therapeutic doses in reducing the secretory activity of a hyperfunctioning adenoma. Presumably it should prove effective though the failure of roentgen irradiation in the 2 cases in which this latter agent was employed suggests that larger doses of radioactive iodine might be needed than in Graves' disease with diffuse hyperplastic goiter. It is not surprising that thiouracil was effective in lowering the metabolic rate in the patient in whom this drug was

[1]Of 82 cases of hyperparathyroidism proved by operation at the Massachusetts General Hospital, 75 have had the localized form of anatomic disorder. In 70, one gland only has shown an anatomic abnormality, and in some of these not even the whole gland has been involved in the disease process; a small rim of uninvolved parathyroid tissue has surrounded the disordered tissue. In 5 of the 75 cases, two glands, rather than only one, have shown changes; the other two glands of each patient were not involved. Because of the localized nature of the disease in these 75 cases the lesion has been considered neoplastic and has been called an adenoma.

In 7 of the 82 cases of hyperparathyroidism the disease process has involved all of the tissue of all 4 of the parathyroid glands and has been termed hyperplasia by some and hypertrophy by others. That the disease process is considered different from that of the localized neoplasia or adenoma is strengthened by the fact that the cell type and arrangement in the hyperplastic glands is clearly distinguishable from those of the cells found in the adenomas.

tried. From a chemical point of view thiouracil should block formation of the thyroid hormone by any cell, neoplastic, as well as hyperplastic and normal (9). The ultimate fate of the adenomatous cell after both radioactive iodine and thiouracil therapy remains to be established.

SUMMARY

The single adenoma of the thyroid gland causing hyperthyroidism is established as an entity. It is the rare type of pathologic anatomy found in patients with thyrotoxicosis; 10 cases have been encountered in the Thyroid Clinic at the Massachusetts General Hospital in the last 10 years. Proof of its existence in a patient depends upon the absence of other diseased thyroid tissue, the presence of gross anatomic atrophy and of physiologic inactivity of the uninvolved thyroid tissue and relief of the excessive function upon its removal.

The atrophy of the uninvolved thyroid tissue can be suspected on physical examination but should always be recognized at operation and undue resection of it avoided.

The physiologic activity of the adenoma and uninvolved thyroid gland has been compared by the ability of explanted thyroid tissue to inactivate thyroid stimulating hormone and by the avidity of the thyroid for tracer doses of radioactive iodine. Both tests have shown activity of the adenoma comparable to that found in the hyperplasia of the common type of thyrotoxicosis and absence of function of the uninvolved tissue.

The absorption of tracer doses of radioactive iodine by single adenomas not associated with hyperthyroidism suggests that the secretory activity of adenomatous tissue varies over a wide range and that the presence of thyrotoxicosis in a patient depends upon the degree of activity and size of the adenoma. The activity of the accompanying uninvolved tissue varies inversely and is depressed when that of the adenomatous approaches an excessive amount.

The relative effectiveness of thiouracil and radioactive iodine compared with surgery in relieving the hyperfunction associated with this pathologic type, and the eventual fate of the localized neoplastic process when these two drugs are employed, has not been established.

ADDENDUM.—Since this manuscript was submitted for publication the distribution of radioactive iodine in the adenoma compared with that in the atrophic uninvolved tissue has been observed in 2 additional patients with thyrotoxicosis due to a hyperfunctioning single adenoma. The first patient, a girl of 17 years, had a mild degree of thyrotoxicosis; the adenoma contained 8.3 per cent per gram of the radioactive iodine given, the uninvolved thyroid tissues 0.059 per cent per gram and a lymph node 0.014 per cent per gram. The second patient, a woman of 55 years, had a moderate but crippling degree of thyrotoxicosis; the adenoma contained 0.88 per cent per gram of the radioactive iodine, the uninvolved tissue 0.37 per cent per gram. Removal of the single adenoma and resection of 1 gram only of the uninvolved tissue for analysis, resulted in relief of the thyrotoxicosis in both cases.

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RESECTION OF THE COMMON HEPATIC DUCT FOR PAPILLARY ADENOCARCINOMA

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A PRIMARY carcinoma of the extrahepatic bile ducts, especially if those of the ampulla of Vater are excluded, is an extremely rare finding. Pathologically, there are two types, the nodular and the papillary, and of these the latter is most infrequent, comprising only about 10 per cent of the total. All writers agree that papillomatous growths in the bile ducts will obstruct the lumen before penetrating the wall of the duct; in brief, they probably remain as a local lesion long enough to produce definite symptoms before metastases take place. Marshall, found 4 papillary carcinomas of the extrahepatic ducts in a series of 49 carcinomas of these structures, and stated that most papillary growths in this region would prove malignant on section.

Males (60%) more often than females are affected with carcinoma of the bile ducts, but females are more often affected with carcinoma of the gall bladder (80%) (1). The average age of individuals with bile duct carcinoma is 55.5 years. Carcinoma of the gall bladder is said to be four times as common as carcinoma of the bile ducts.

In the series presented in Table I (1), if one includes under one heading all the tumors arising from the common bile duct including the ampulla, then the common bile duct is the most frequent site, with 210; next, is the junction of the three ducts—cystic, common, and hepatic duct with 124. The hepatic ducts, right, left, and common, present the next most frequent site with 87, and the cystic duct is the least frequent site. We were able to find only 21 cases in which the common hepatic duct alone was involved, 19 reported by Rolleston and McNee, and 2 by Marshall, but this figure may not be accurate.

Symptoms. Jaundice is present in 100 per cent of cases. Complete biliary obstruction is present in over 90 per cent. The onset is acute in almost 90 per cent. Loss of weight and strength also occurs in nearly all, if not all, patients. Pain is present in about 52 per cent. Chills, elevation of temperature, vomiting, diarrhea, and pruritis are common. Ordinarily no mass is palpable in region of primary tumor, the liver is enlarged in 68 per cent and the gall bladder in 26 per cent, and about 50 per cent have ascites.

CASE REPORT

Mr. C. S. C., white, aged 73 years, entered Heights Hospital February 2, 1946. His chief complaints were: marked jaundice, widespread itching, loss of 20 to 30 pounds in weight, persistent diarrhea. His present illness began about 8 weeks before admission, with indigestion and a mild burning and bubbling in his stomach. After a week of this, he began to develop a yellow color and his stools became rather light in appearance. The jaundice was first noted December 20, 1945, and gradually became more pronounced. At no time was there any definite pain in the abdomen. There was no fever, no chills, no nausea or vomiting. Three weeks after jaundice appeared, itching was rather marked. Until admission to hospital he had a rather continuous diarrhea and lost considerable weight, probably 20 to 30 pounds, but felt hungry and ate all types of food during the present illness.

He had usual childhood diseases, and typhoid at 27 years. He had had an appendectomy 10 years before, and 5 years before had had 18 skin lesions, stated to be "skin cancers," removed from back of neck and right ear. None of these had recurred.

His father died at 82 years, cause unknown. Mother died at 69 of hypertension. One brother died at 58 of heart attack, and two sisters, ages unknown, living, one sister with tuberculosis. No history of cancer or tuberculosis otherwise in family.

Physical examination revealed a thin, emaciated white man, with marked icteric tint to skin and sclera, many skin abrasions as result of scratching. Patient was mentally alert, not toxic, very co-operative in all respects. His blood pressure was 140/90; the heart action was a little irregular; there was no cardiac enlargement, but there was a rather loud systolic murmur at the apex. The lungs were clear. The abdomen was markedly scaphoid, and the liver was enlarged about three fingersbreadth below the costal margin. The spleen was not palpable. No other masses other than the enlarged liver were noted. Rectal examination was essentially negative,

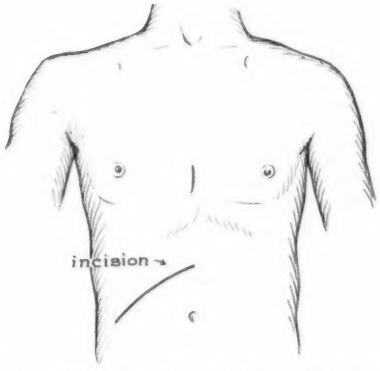

Fig. 1. The upper oblique incision (Singleton).

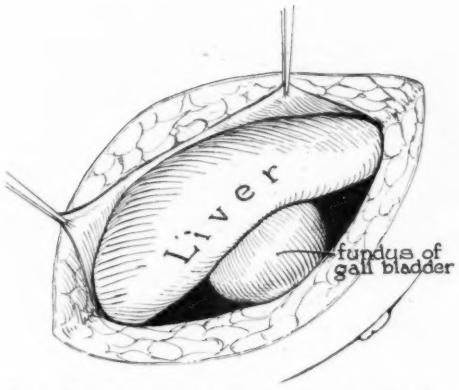

Fig. 2. Greatly enlarged liver and distended gall bladder.

no nodules on rectal shelf. The temperature was 98 degrees, pulse good volume, slightly irregular.

Laboratory examination on February 4, 1946 showed: urine—dark amber, clear, alkaline, specific gravity 1022, albumen 0, sugar 0, blood 0, epithelium cells rare, casts granular rare, bile present. Blood—red blood count, 4,040,000, hemoglobin,, 80 per cent Sahli, white blood count, 5,800, polymorphonuclears, 58, lymphocytes, 40, juveniles, 2, icterus index, 100.

He was seen in consultation February 3, 1946 by Dr. E. K. Doak, whose impression was that it was a malignant condition causing obstruction of the biliary tract and advised a gastrointestinal series. This was done by Dr. B. T. Vanzant and was essentially negative except for a large number of diverticula in the lower sigmoid. His report is as follows: "February 4, 1946, G. I. Series: Fluoroscopically: the upper half of the stomach is a mere tube with greatly thickened longitudinal musosal folds. The material passes immediately into the duodenum, and on into the small intestines.

"At the end of four hours: stomach is practically empty. Residue shows an extremely ragged lake-like residue with all the opaque material in the ischium and first portion of duodenum.

"Six hour plate: terminal ileum and the first portion of ascending colon contains all material.

"Twenty-four hour plate: colon is empty, except for small amount in the transverse colon. A small retention pocket in the caecum, a slightly larger retention pocket in the splenic flexure with only a moderate amount in the sigmoid.

"In the six hour plate we notice in the right lower quadrant, a very large number of shot-like pockets, evidently in the wall of the small intestine; and in the twenty four hour plate, the lower sigmoid shows a large number of diverticulae.

"The case is apparently one of generalized hypermotility and general spasticity. Unable to detect any definite anatomical lesion.

"Would suggest the possibility of a very marked avitaminosis of the pellagra type."

We believed that it was most likely a case of carcinoma of the head of the pancreas and so advised our patient. It was decided that the abdomen should be explored in the hope that his condition could be improved, and he was therefore prepared for surgery. He was given daily doses of vitamin K with bile salts, large amounts of vitamins A and D and B complex, also 2 cubic centimeters of crude

TABLE I.—LOCATION OF EXTRABILIARY DUCT TUMORS IN 484 PATIENTS

Author	Date	Hepatic	Cystic	Junction of 3 ducts	Suprapancreatic	Pancreatic	Duodenal
Donati	1905		32	37		48	
Rolleston and McNee	1929	23	7	28	11		23
Shapiro and Lifvendahl	1931	2	2		3		4
Judd and Gray	1932	8	7			28	
Walters and Olsen	1935	10	7			33	
Dick	1930	2	3				13
Stewart, Lieber, and Morgan	1940	35		48		21	
Marshall	1932	7	5	11	11		15
Totals		87	63	124	25	130	55

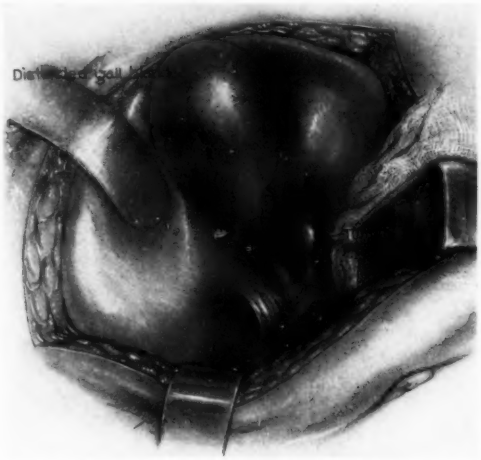

Fig. 3. Tumor shown in common hepatic duct extending almost to bifurcation of duct.

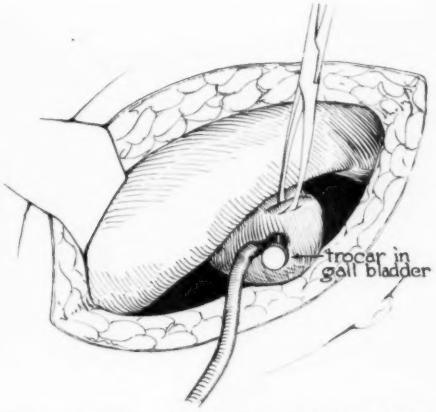

Fig. 4. Aspiration of distended gall bladder; black bile obtained.

liver intramuscularly. He was also given digitalis for 3 days before operation, plus two transfusions of 500 cubic centimeters each. Operation was done February 15, 1946. Pentothal was used for induction.

An upper oblique incision was used (Fig. 1), transecting the right rectus muscle. When the abdomen was opened the liver was seen to be greatly enlarged with rounded edges, greenish black in color, and the gall bladder to be enormously distended (Fig. 2), at least four or five times normal size, but of a rather normal color and thickness. We then examined the pancreas, which we fully expected to find hard and enlarged, but to our amazement it felt entirely normal. This fact was so astonishing that we could hardly believe it, and we incised the peritoneum lateral to the duodenum, mobilized the duodenum and carefully explored the entire retroduodenal portion of the common duct and found it, as well as the adjacent pancreas, entirely normal in all respects. Then a small oblong mass, about the size of a large pecan (Fig. 3), was noted up toward the fissure of the liver. We decided that it must be a stone or tumor in the common hepatic duct. A small nick was made in it and confirmed the fact that it was the duct, and that a tumor was present therein.

No nodules could be felt in the liver or adjacent structures, and it was decided to resect the tumor-bearing section of the duct. To facilitate exposure, the gall bladder was aspirated through the fundus (Fig. 4), and a large amount of black bile was removed. Then the duct was cut across transversely as far above the tumor as possible; this was right against the liver (Fig. 5). It was then cut through below the tumor, and the distal end closed over with a continuous stitch of No. 0 chromic plus an ordinary tie below this suture line (Fig. 6.). A lymph node adjacent to the tumor was also removed for examination.

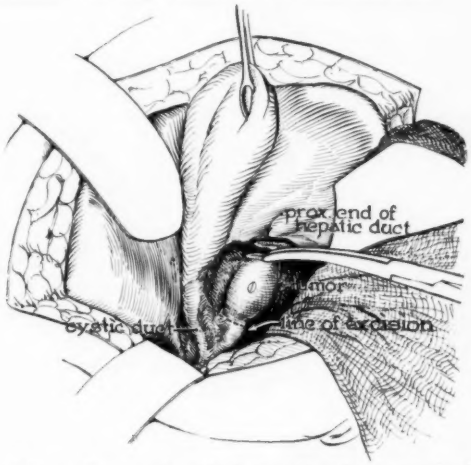

Fig. 5. Common hepatic duct sectioned near proximal end. Distal line of section indicated by dotted line.

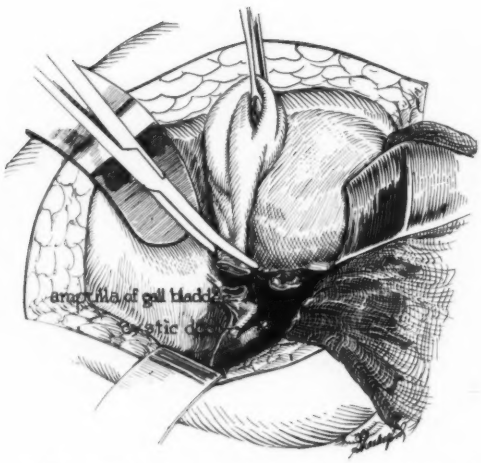

Fig. 6. Distal end of hepatic duct closed, proximal end open. Gall bladder sectioned through ampulla, distal edge not crushed.

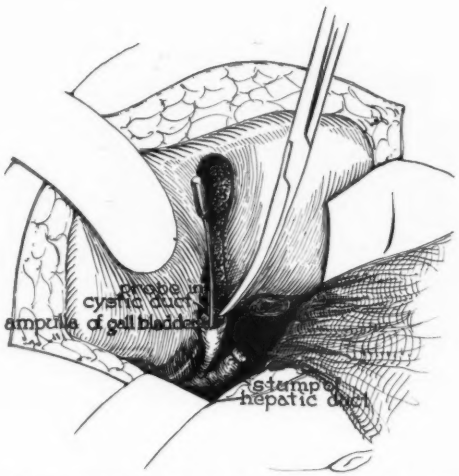

Fig. 7. Probing cystic duct in order to determine patency should be carried out before removal of the gall bladder.

The problem of bridging the gap between the cut ends of the common hepatic duct was managed by using the cystic duct and the ampulla of the gall bladder to provide a mucous membrane lined tube and a tube already accustomed to handling biliary drainage which permitted little chance for later stricture development.

A forceps was applied across the ampulla of the gall bladder, and it was cut across proximal to this (Fig. 6). The edge not crushed by the forceps was used for the anastomosis. A probe was then passed through the ampulla, down the cystic duct and the common duct into the duodenum doubly to assure the patency of the entire tract (Fig. 7.). This flanged out ampulla (which was assurance against later stricture formation) was then sutured to the open end of the common hepatic duct, *everting* rather than inverting the edges (Fig. 8a), a further step in preventing stricture formation, with 0 chromic on atraumatic needles. A small catheter, size 12 French, was placed so that its bell end opened into the proximal end of the common hepatic duct, and it was brought out through a tiny incision in the ampullary portion (Fig. 8a). The remainder of the gall bladder was then removed and bed sutured over (Fig. 8b).

Three Penrose drains were placed and brought out through the main incision. The catheter was brought through the main incision also, but about an inch away from these drains.

The tumor filled the entire section of duct except for a very small space through which a small probe could be passed. The growth of the tumor was producing a very marked intraluminal pressure as it bulged outward.

The tumor was examined by Dr. A. H. Braden, whose report is as follows:

"An irregular mass from the hepatic duct measuring 2.5 by 2 cms. The color is brownish and the tissue is moderately firm with softer areas in the center. A lymph gland which measures 7 by 4 by 5 mms. is fairly regular in shape and is rather soft. Microscopically sections were made from both extremities. Some of the sections show rather large gland acini lined by single layers of cuboidal cells filled with mucinous material (Figs. 9 and 10). Other sections show atypical gland acini that are lined by hyperplastic cells that are irregular in size and shape with mitotic figures that are atypical. The arrangement is quite frequently papillomatous (Figs. 11 and 12). The wall is not demarcated other than a connective issue band between the glandular tissue. Sections from the lymph node show no evidence of metastasis. Diagnosis: papillary adenocracinoma, grade II."

The gall bladder, aside from its marked distention, was normal. He made a good recovery, and the

Fig. 8. a, left, Anastomosis of ampulla to proximal end of common hepatic duct. Note eversion of edges, catheter drain. b, Completed operation.

only complication was a failure of the skin edges to unite. The deeper layers all held, he had no hernia, but a secondary closure of the skin edges was necessary. Highest postoperative temperature was 99.8.

Date	Icterus index	Stools (bile) Albumen globulin	Urine (bile)
2- 2-46	100		+
2-15-46	Operation		
2-16-46	80	o	+
2-18-46	80		+
2-20-46		o	
2-21-46	70		
Total protein		6.8	
Albumen		5.3	
Globulin		1.5	
Albumen-globulin ratio		3.1	
2-26-46	66		
3-18-46	Catheter removed		
3-20-46		+	
3-21-46	25	+	
3-25-46	22		o

On March 5 the biliary system was injected through the catheter, and besides outlining the intrahepatic system also demonstrated that the media passed on into the duodenum (Fig. 13). At this time his urine still contained bile, and the stools were negative for bile. Report of the x-ray examination for March 5, 1946 was:

"Beautiful filling of all the hepatic ducts. Common duct is open and material flows freely into duodenum."

On March 16 another injection was done, demonstrating the same situation. X-ray report for March 16, 1946 (Fig. 14) was:

"Very excellent injection of the biliary tree. The material flows into the duodenum."

He continued to improve, the external biliary drainage became much less 36 hours after the catheter was removed on March 18, and on March 22 he was allowed up in a wheelchair. His stools were beginning to have a more normal color, his appetite was very good, and he felt himself gaining strength every day. By March 25 there was almost no drainage, and he was allowed to go home.

This case has unusual features:

1. With marked loss of weight and strength, he still had a good blood count.

2. His appetite was never bad, even from the beginning.

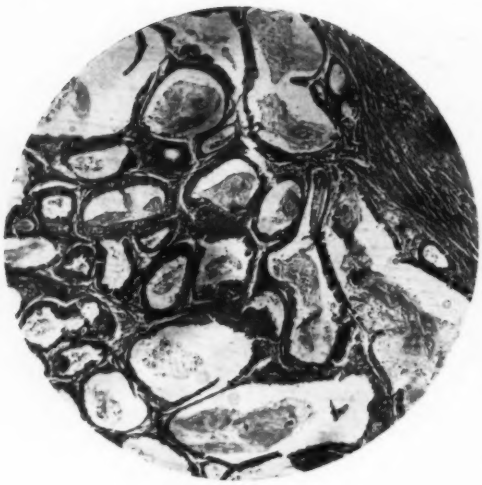

Fig. 9. Low power.

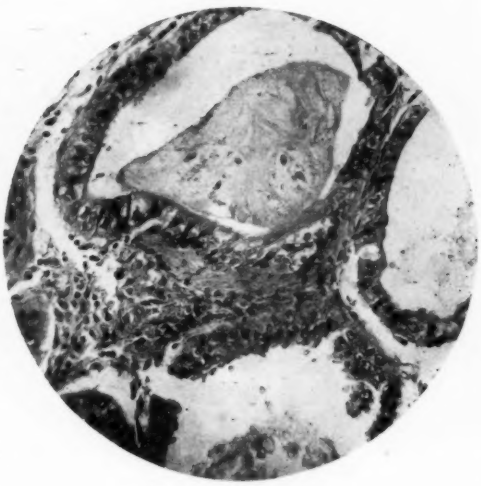

Fig. 10. High power.

3. We wonder if any connection exists between the numerous "skin cancers" removed 5 years before. Once before one of us (J.P.B.) saw an elderly man develop primary carcinoma of the liver 10 years after having had a basal cell carcinoma of the face removed with radium.

We believe that the obstruction was complete but that at times a little bile was forced through the narrow tract by pressure from the liver, otherwise the bile in the gall bladder would have been "white bile" instead of the black.

If no bile at all had reached the intestine he would have had marked anorexia, but this was not the case.

We are unable to explain the enormously distended gall bladder. According to Cour-

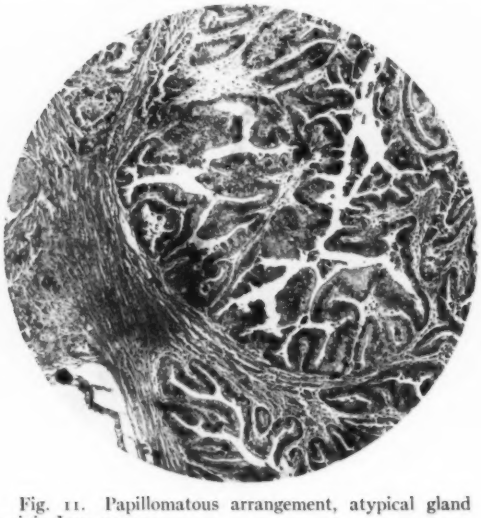

Fig. 11. Papillomatous arrangement, atypical gland acini. Low power.

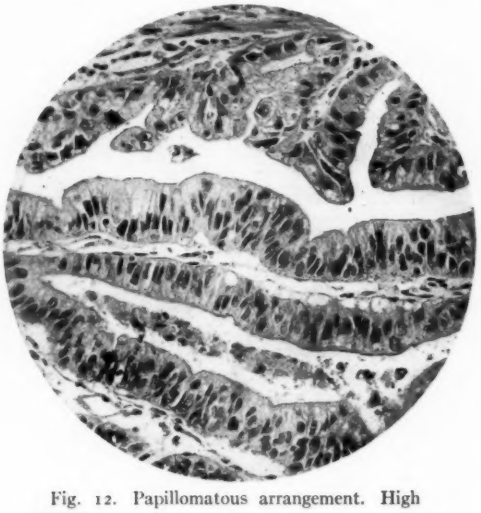

Fig. 12. Papillomatous arrangement. High power.

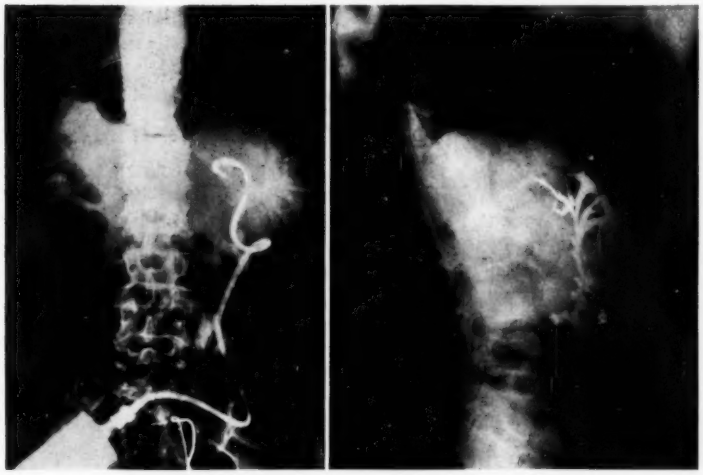

Fig. 13, left. Injection of biliary system. Note passage of media into duodenum.
Fig. 14. Note injection of cystic and common bile ducts. Media passes into duodenum.

voisier's law, extrinsic pressure on the ducts (and usually pressure exerted at a point distal to the junction of cystic and hepatic ducts) produces a distended gall bladder. Here, the pressure was intrinsic and was at a point well proximal to the junction of cystic and hepatic duct. It was evident that bile was getting by in tiny amounts and being stored up in the gall bladder, but the gall bladder was not contracting and emptying itself through the sphincter of Oddi very well. Perhaps the abnormal pressure in the hepatic duct in some way interfered with the reciprocal autonomic regulation of the gall bladder-sphincter of Oddi mechanism.

The cystic duct here was quite small, but a 3 millimeter dilator could be passed through it, and we depended on the inherent ability of the duct as a mucous membrane lined tube to dilate sufficiently to carry the total biliary stream. The correctness of this assumption was demonstrated clinically when, at removal of the catheter, the external drainage promptly ceased, the urine cleared, and the stools regained their normal color. This characteristic ability of a mucous membrane lined channel to dilate and thus carry a heavier load than nature originally intended should always be remembered in dealing with similar problems.

The use of the ampulla of the gall bladder is noteworthy. Every end-to-end anastomosis, especially when the ends are inverted, as in intestinal work, has a certain amount of narrowing due to slight septum formatin by the inverted portion, plus a later contraction of the circular line of union. Therefore we used a section of the gall bladder with at least twice the cross section diameter of the stump of the duct to which it would be joined. The edges were everted, and thus no septum or spur whatever was formed. So far as we know, this procedure has not been previously reported.

On July 20, 1946 a follow-up revealed our patient in good condition, his wound well healed, no jaundice, and a good appetite, and he had gained 18 pounds since leaving the hospital March 25, 1946.

In reviewing this case, attention is called to an alternate method that might be used in a similar case. The method presented depends upon a patent cystic duct. Most cystic ducts are patent, yet the possibility of a closed duct must be remembered. Where a diagnosis of hepatic duct tumor has been made at operation and the gall bladder present and healthy, the following method of attack is suggested:

Aspirate the gall bladder, preferably near, or at, the fundus.

Probe the cystic duct either through the aspiration opening in the gall bladder or through a small opening in the ampullary region, and if patent, the method already presented may be used if desired, but if for any reason it is not applicable the following method may be employed:

Resect the hepatic duct tumor, but make every effort not to damge either the cystic or hepatic artery.

Do not close the distal end of severed hepatic duct.

Beginning at the fundus, dissect the gall bladder away from its bed, protecting the cystic artery at the base of the "flap."

Anastomose the fundus of gall bladder to proximal end of hepatic duct.

Implant distal end of hepatic duct into side of gall bladder, which will probably be a little above the ampullary region. If the gall bladder should be half as large as in the case presented, no trouble will be experienced.

Put catheter or soft T-tube in gall bladder.

SUMMARY

A case of papillary adenocarcinoma of the common hepatic duct, with successful resection, has been presented. A method of utilizing the ampulla of the gall bladder and cystic duct as a substitute for the common hepatic duct has been demonstrated.

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MASSIVE ILIAC BONE GRAFTS IN THE TREATMENT OF UNUNITED FRACTURES AND LARGE DEFECTS OF LONG BONES; THE COMBINED BONE GRAFT-METALLIC PLATE TECHNIQUE

An Analysis of 91 Operations in 85 Patients

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THIS is a further appraisal of massive iliac bone grafts in the treatment of ununited fractures of long bones, with or without defects and of massive bone defects in the presence of union. Further experience with 85 patients in whom 91 bone graft operations were performed has indicated to us the need for certain variations in technique, the wide application of iliac bone as graft material, the specific indications for the use of cortical bone, and certain hazards involved in this type of reconstructive surgery in battle casualties. In effect, this contribution is a final analysis, since all of the patients in this study have either been separated from military service or have been transferred from our care to other military hospitals.

The material reported herein has been collected and observed over an 18 months period terminating on March 15, 1946, and will be discussed under the following headings:

1. Experiences with the use of iliac bone as massive bone grafts; the specific indications in which cortical bone is preferable to iliac bone as graft material.
2. The specific place for plate fixation in combination with bone grafts; fixation by multiple screws in oblique fractures.
3. Modifications and variations in the technique of the combined graft-plate method and of bone grafting without plate fixation.
4. Incidence and factors involved in failure of the graft operation.
5. Incidence and factors involved in the occurrence of postoperative infection; fate of iliac grafts in the presence of infection.

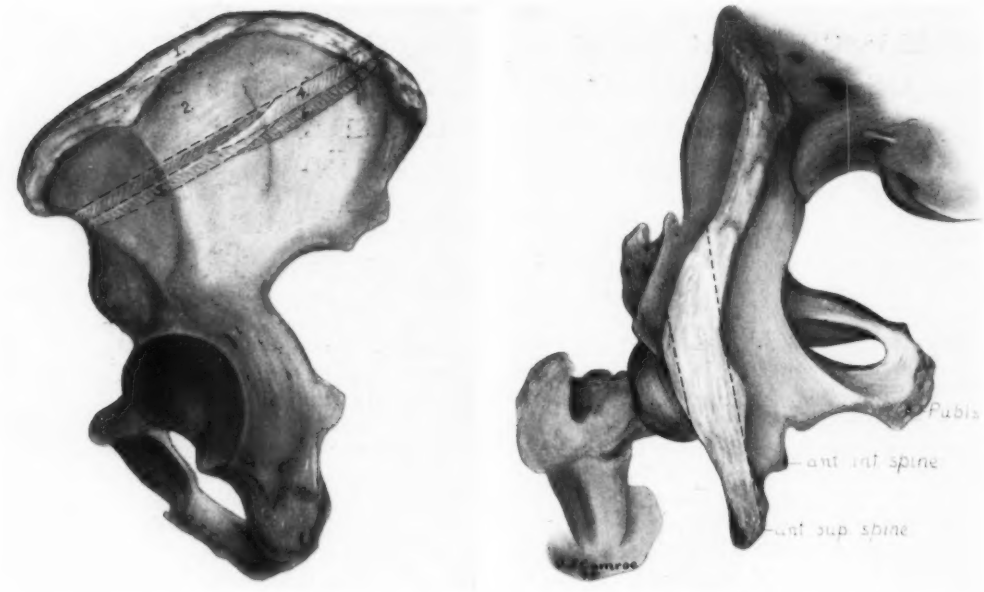
1. Experiences with the use of iliac bone as massive grafts; the specific indications in which cortical bone is preferable to iliac bone as graft material. There has been considerable controversy over the relative merits of cortical versus iliac bone as graft material, the essence of which seems to be that while bone from the ilium is more readily revascularized and incorporated into the host bone because of its cancellous nature, tibial bone has the advantage of being rigid enough to give good internal fixation to the host bone when fixed to it with screws. The authors feel, however, that what iliac bone lacks in rigidity is more than compensated for by its superior osteogenic qualities and that the simple addition of a plate imparts the required stability.

The disadvantages of tibial grafts are: delayed incorporation into the host bone, fracture in the donor bone, a complication which may occur after removal of a surprisingly small graft, fracture of the graft after implantation unless it be protected by the addition of a plate, and limitation of the amount of bone obtainable unless both tibias are used.

Iliac bone, on the other hand has none of these disadvantages, and has the advantage of rapid incorporation as well as a relatively unlimited supply of graft material. Single grafts up to 5 inches (12.5 cm.) in length and 1 inch (2.5 cm.) or more in width as well as numerous sliver and chip grafts are available from one ilium and no limp or other untoward effect has been observed even when both iliac crests have been used.

Presented before the Committe on Fractures and other Traumas of the American College of Surgeons at Vaughan General Hospital, Hines, Illinois, January 18, 1946.

From the Section of Orthopedic Surgery, Vaughan General Hospital, Hines, Illinois; Dr. Horwitz, formerly chief and Dr. Lambert, assistant chief.



a b

Fig. 1, a and b. Diagrammatic representation of method of sectioning the grafts from the iliac wing with the electric saw. Graft 2 is the major onlay graft, while the other segments are used as intramedullary grafts and extracortical sliver grafts. The length of the graft is exaggerated in the drawing for the usual 6 inch incision. Incisions exceeding this length have been used in order to remove large amounts of graft material from the major portion of the iliac wing.

The experience that iliac bone is more rapidly incorporated into the host bone than cortical bone when used as graft material, as reported in the author's initial communication[1], has been sustained. This fact has not only been interpreted on the basis of the roentgenographic features of graft incorporation, but from the gross and microscopical features of graft specimens removed at the time of reoperation in 6 patients. These observations have served to sustain the concept that cancellous bone by the nature of its architecture encourages more rapid invasion and replacement by new bone than does cortical bone. This has held true not only in the instance of small chip and sliver grafts which have been used to fill in bone cavities and to reinforce cortical grafts, but in our cases where the cancellous grafts have been massive. The technique of exposure of the iliac wing by liberal stripping subperiosteally of soft tissues from both the external and internal aspects, has permitted the removal of massive grafts which are easily shaped with the electric saw to bridge ununited fractures and to fill large defects (Fig. 1, a and b). This is further facilitated by the control of bleeding with the electric cautery, by the use of the electric knife and by the removal of the graft with the longitudinal attachment of the Luck saw.

In discussing graft material, the authors are fully aware that no bone graft specimen is wholly cancellous or cortical bone. The massive iliac graft, while it is mainly cancellous in structure, has an inner and outer table of cortical bone which, in effect, lend to the stability of this type of graft, while a cortical graft from the femur or tibia may have a layer of cancellous bone on its deep surface and a variable amount at its end depending on how much of the metaphysis of the donor area has been removed.

Those who have used cortical grafts, especially to bridge gaps, know that a critical

[1]Horwitz, T., and Lambert, R. G. J. Bone Surg., 1945, 27: 637–644.

period exists after the third month at which time the center of the graft may begin to resorb and may disappear or be the site of a fracture. In this type of graft this phase of resorption is easily detected on roentgenograms; the cortical graft appears denser and whiter than the adjacent host bone. The same phenomenon may occur with massive iliac grafts, although this is harder to detect on roentgenograms where the cancellous graft fails to stand out in contrast to the surrounding bone. In 3 cases, 1 with a nonunion of both bones of the midforearm, another of the surgical neck of the humerus, and the third, involving the upper third of the femur, dissolution of the central portion of the massive iliac graft appeared between the third and fourth postoperative month, with recurrence of nonunion, while in a fourth case, a nonunion of the forearm recurred after the use of an iliac graft with a plate which had bridged the fracture inadequately, the graft resorbing in its center in like manner. In other words, although cancellous bone is more rapidly incorporated into host bone when used as graft material, its central portion, where the process of creeping substitution and the replacement of new bone by mature bone is last manifest, represents a site of structural weakness which requires prolonged and rigid support and protection. This is especially true where the graft is bridging a gap and is surrounded in this region solely by soft tissues. Rigid fixation cannot be obtained by plaster of Paris alone, no matter how accurately applied, and it is best secured by the use of a metal plate. Such additional plate fixation is absolutely necessary in the grafting of single long bones, as the femur and humerus, and particularly in their upper and middle thirds where the stress of the lever action of the extremity is most vicious, and in the forearm and leg, when both long bones are ununited. In the forearm and leg, where one of the long bones is intact, the splintage afforded by the intact component will suffice with the usual method of fixation of the graft and a plate need not be utilized. Recurrence of nonunion has occurred in this group of patients, excluding those failures incidental to postoperative infection, as a result of failure to recognize two essential mechanical

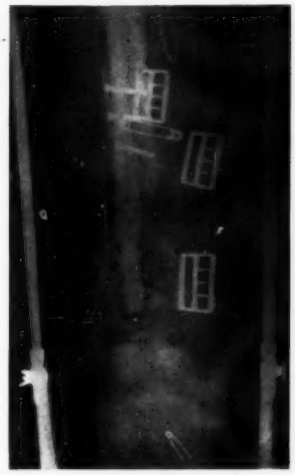


Fig. 2. Patient sustained a compound fracture of the right femur in a motorcycle accident. Reconstruction of a nonunion with gap-defect was performed by means of a massive cortical graft from the left tibia, which was affixed as an onlay to the proximal femoral fragment with three stainless steel screws after its distal end had been driven into and well impacted within the substance of the short atrophic distal fragment. The use of a metallic plate was mechanically impossible in this subject. The anteroposterior roentgenographic view, made 2 weeks postoperatively and just prior to his transfer to another military hospital, is illustrated. The limb was protected in balanced suspension with skeletal traction through the upper end of the tibia at the time that this examination was made.

principles early in this study, i.e., the need for metallic plate fixation in certain instances as defined above and the need for rigid fixation by plates of adequate length.

On the other hand, iliac bone, when it includes one and especially both tables, has sufficient stability for use alone and without plate fixation, as in the treatment of ununited fractures of a single forearm bone or of the tibia in the presence of an intact fibula, and when it is fashioned from the iliac crest and includes three cortical surfaces—the crest and both tables—it is as rigid as a segment of cortical bone of similar dimensions.

Cortical bone must be used in selected cases:

a. Where the graft is necessary to bridge a considerable gap as in the femur and must measure in excess of 5 inches, it is obligatory that cortical bone be used. The osteogenic properties of such massive cortical grafts will

Fig. 3, a and b. Patient sustained a severe compound comminuted fracture of the right femur as the result of enemy shell fire. An onlay iliac graft, fixed with stainless steel screws, was employed to bridge the 3 inch (7.5 cm.) defect and the interval was packed with slivers of iliac bone. The wound healed *per primam*, but despite adequate protection of the extremity in balanced suspension and skeletal traction, the center of the graft proceeded to resorb with recurrence of nonunion 6 months postoperatively. A second graft, obtained from the left tibia, was applied and rigid fixation secured by the application of a stainless steel plate; a, left, is an anteroposterior roentgenogram of the femur just prior to the second grafting and, b, right, is an anteroposterior view made 2 weeks following this operation. The limb was protected in balanced suspension with skeletal traction through the upper end of the tibia at the time this report was completed.

be enhanced by the additional use of slivers of cancellous bone removed from the ilium. This has been the experience in 3 patients with ununited fractures of the femur and with massive defects. In one of these, dual tibial grafts were applied and transfixed to each other and to the atrophic ends of the femoral fragments, and further fixation was obtained by a long metal plate. In the second case, the massive cortical graft, removed from the tibia, was transfixed to the proximal fragment with three screws and its distal end was driven into the spongy substance of the short distal fragment for a distance of about 2 inches (Fig. 2). In the third case, a massive iliac graft resorbed in its central portion, with recurrence of nonunion (Fig. 3a). At operation, the defect was bridged and rigidly immobilized with a metallic plate and a massive cortical graft was applied (Fig. 3b).

In a fourth instance where a gap of 5 inches existed in the upper end of the humerus with loss of the humeral head and entire glenoid, the shaft of one fibula was used between the remains of the scapula and the humeral shaft, being driven into the humeral fragment distally and transfixed at its proximal forked extremity with one screw. In this case resorption occurred in the center of the graft with a pathologic fracture, even though the arm appeared adequately protected in plaster of Paris. At the time of regrafting the viable fibular fragments were found to be firmly incorporated into the host bone and the pathologic fracture was bridged by a tibial graft held with two screws above and two below the

fracture site. Union of the pathologic fracture has occurred, and the tibial graft is becoming incorporated into the substance of the original fibular graft (Fig. 4).

b. Cortical bone must be used where a rigid piece of bone which is perfectly straight is required as graft material. For instance, in 1 patient two cortical grafts were introduced across an ununited fracture of the neck of the femur with viable head, one above and the other below an accurately placed Smith-Peterson nail. Since the grafts were applied through the greater trochanter, channels having been drilled accurately under roentgenographic control, it was essential to use an absolutely straight graft of rigid nature which would tolerate introduction with a mallet, and cortical bone was felt to be most suitable. The writers have had the same experience with the use of cortical grafts in the Brittain type of hip fusion although this type of case is not included in this report.

2. The specific place for plate fixation in combination with iliac grafts; fixation by multiple screws in oblique fractures. The specific purpose of a metallic plate is to give rigid fixation to the fracture and to protect the graft throughout its period of incorporation. When the iliac graft is applied across the fracture site or defect and is transfixed with screws through graft and both cortices of the host bone and *at right angles* to the plate and its screws, added fixation is insured.[1]

The duration of the period of external fixation varies with each case. Much depends upon the degree of stability of the fracture as determined preoperatively, the method of internal fixation employed at the time of operation, and the size and nature of the defect, for the greater the defect the longer the period required for complete revitalization of the graft and the greater the danger of its resorption or fracture. The degree and length of protection will also depend upon the site of the defect. The demands for protection are greatest for a weight bearing bone (femur or tibia) and for a single bone as the femur or humerus, particularly in their middle and upper thirds, or for double bone involvement in the forearm and leg. An intact radius, ulna, or fibula offers considerable protection to a fracture of the adjacent bone.

[1]This may be varied in the instance of extremely porotic bone wherein the graft is applied across the fracture site directly opposite the plate, permitting a more secure bony purchase for the screws fixing the plate.

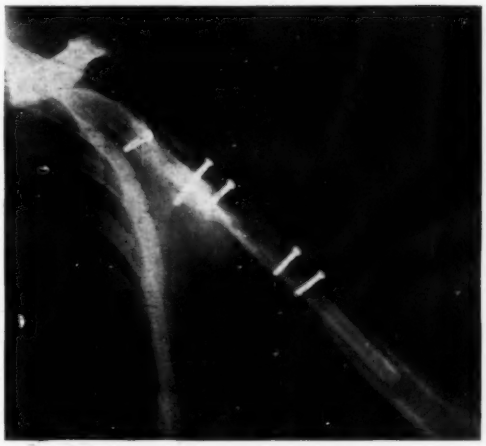


Fig. 4. Enormous defect in the rigid humerus following a compound comminuted fracture incurred in battle, with loss of the proximal half of the humerus and the entire shoulder joint. At the first operation a fibular graft was inserted between the scapular blade and the distal humeral fragment, but the center of this graft, despite protection of the extremity in plaster of Paris, resorbed in its center with the appearance of a pathologic fracture 6 months postoperatively. The illustration shows the roentgenographic appearance 3 months following the second operation at which time the fibular fragments were reduced and immobilized by an onlay tibial graft. The fibula now appears to be well united and the tibial graft is undergoing incorporation into the adjacent bone. The extremity was protected in a plaster-of-Paris shoulder spica at the time this report was completed.

In the instance of ununited fractures of the femur, plate-graft fixation has been rigid enough to warrant the elimination of postoperative plaster-of-Paris fixation and the extremity has been protected by skeletal traction in balanced suspension. Such patients have been up in an ischial weight bearing brace 4 months postoperatively, with full weight bearing by the 6th month and brace support has been discarded between the 9th and 12th month postoperatively (Fig. 5 a and b, Fig. 6 a and b). Patients with ununited fractures of the tibia treated by the graft-plate technique have often borne weight in a walking cast between the 3rd and 4th postoperative month and this has been followed by brace protection for 6 months or, if there has

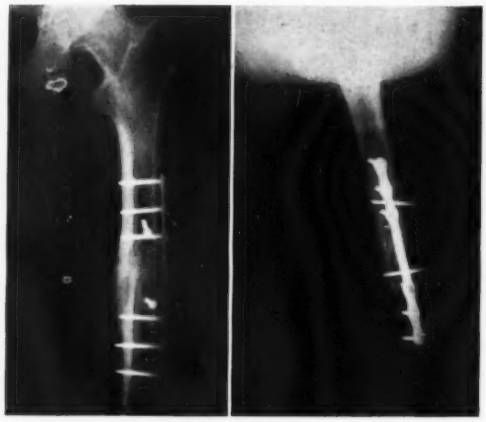


Fig. 5, a and b. Simple fracture of the left femur which was treated by open reduction and plate fixation 6 weeks after injury by a falling log. Delayed union with an interval gap between the fragment ends and with little callus formation was evident 6 months later. An iliac bone graft was applied and the metallic plate left *in situ*. a and b, Anteroposterior and lateral roentgenograms of the femur made one year postoperatively. The medullary canal is reforming, there is thorough incorporation of the bone graft and union is solid. Note how the superficial portion of the massive graft has resorbed, as evidenced by some protrusion of the screws and it is for this reason that the operative technique has been modified to include countersinking of the main graft. Brace support was eliminated in this case 9 months postoperatively.

Fig. 6, a and b. Compound comminuted fracture of the right femur incurred in battle with resultant nonunion which was treated by the iliac graft-metallic plate operation 7½ months after the initial injury and 6 months following cessation of all drainage. a and b, Anteroposterior and lateral roentgenograms made 1 year postoperatively. The graft is completely incorporated into the host bone, there is solid union of the fracture, and the medullary canal is reforming. Brace discarded in this case 9 months postoperatively.

been much bony defect, for 9 months. Fractures of the upper extremity have been mobilized at the end of 3 months, being protected in an abduction cast or brace when the fracture involved the upper third of the humerus or by a bivalved hanging cast for fractures distal to this region.

It is the experience of the writers that the use of a plate in addition to the bone graft is absolutely essential in the surgery of ununited fractures of solitary long bones such as the femur and humerus, particularly in their upper thirds where the lever action of the extremity is most vicious. Nonunions have recurred in one case in the surgical neck of the humerus and in another in the upper third of the femur following bone grafts with simple screw fixation, even though the humerus case appeared adequately protected in a plaster-of-Paris shoulder spica and the femur was still supported in traction-suspension. Even in the instance of massive defects where the union is afforded by a narrow osseous bridge and where this lesion exists in the upper third of the humerus or femur, the authors advocate that a metallic plate be employed in addition to the replacement graft (Fig. 7, a, b and c). In the forearm where both bones are ununited, plating of the ulna in addition to grafts of both radius and ulna is recommended, while in the leg when both tibia and fibula are ununited the plate-graft technique is recommended for the tibia. As noted before, in the forearm if the radius or ulna is intact and in the leg if the fibula is intact, sufficient stability is afforded and a plate need not be used. (Figs. 8, 9).

The greatest problem has been to apply the plate in such a manner as to secure maximum rigidity and, for this reason, since the shape of the fracture gap and the fragment ends varies widely, the site and manner of application of the plate must be varied to conform to the mechanical requirements in each case. It is essential to have a plate that is long enough and to have at least two and preferably three screws fixed firmly above and below the fracture level. In the presence of long bone defects a plate longer than that usually employed for

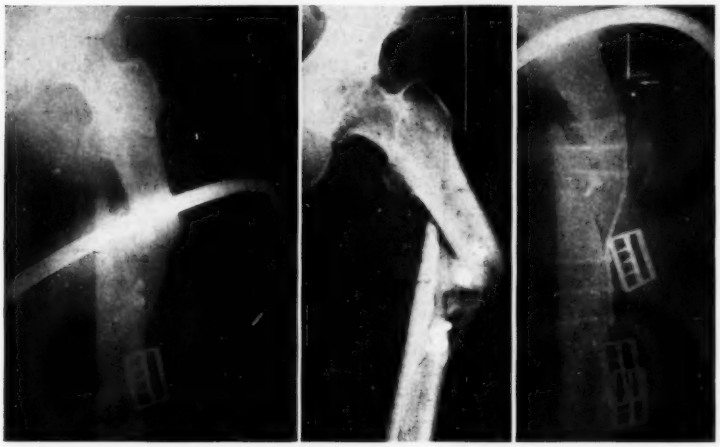


Fig. 7, a, b, and c. This subject incurred a compound comminuted fracture in the upper third of the left femur in battle. Seven months later he presented a large defect at the fracture site with a narrow bony bridge across this defect. Strengthening of the strut by an iliac graft and filling of the defect with slivers of iliac bone was performed, the graft being held securely by two screws above and two screws below as shown in, a, left. Four months later, although the extremity was still protected in balanced suspension and without any history of an injury, a check roentgenogram, b, center, demonstrated increased lateral bowing of the femoral fragments. At reoperation, motion at the fracture site and at the proximal end of the graft was demonstrable. A metallic plate was applied laterally after correction of some of the lateral bowing and the iliac graft was applied to bridge the defect more securely. c, right, Anteroposterior roentgenogram made 2 weeks following the plate-graft operation. The limb was supported in balanced suspension with pin traction through the distal end of the femur at the time this report was completed.

that particular long bone will have to be used. For this reason the longest standard type metal plate utilized for the internal fixation of fractures of the femur is inadequate in the treatment of considerable gaps in that long bone. The authors have had to improvise and fashion plates as long as 9 inches in length in order to bridge certain femoral defects and yet insure adequate proximal and distal screw fixation, and this material has been usually derived from the long arm of the longest Moore-type plate. If the technique herein reported is acceptable it becomes apparent that plates up to at least 10 inches (25 cm.) in length must be manufactured of stainless steel or vitallium, and the authors have called attention to this need. In a nonunion of the subtrochanteric region of the femur, the Blount or Moore plate has served effectively for application of the graft-plate technique in this region.

Another method of internal fixation has been employed which is restricted to the oblique type of ununited fracture and which has permitted the elimination of a plate in such cases at the time of application of the bone graft. The fracture is transfixed, after freshening its surfaces and insuring accurate contact, by two or three screws, and then the graft is applied at right angles in a prepared bed across the fracture and is held by two screws above and two below this site. This technique has been employed in the tibia and ulna, and in the instance of the tibia the graft has been applied, wherever possible, on the fibular side and in the ulna on its radial side.

3. Modifications and variations in the technique of the combined graft-plate method and of bone grafting without plate fixation. While the authors recommend the use of plates and screws as an essential feature of their grafting technique, they are fully aware of the undesirable features of metallic internal fixation. There is no question that once postoperative infection has occurred (and the potentiality

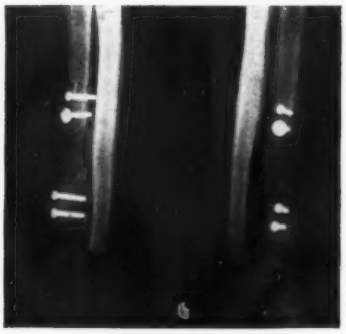


Fig. 8. Compound comminuted fracture of the left radius, incurred in battle, with resultant nonunion and a gap-defect of 2 inches. At operation 6 months following the cessation of all drainage, an iliac graft, shaped to fit the oblique ends of the radial fragments, was interposed and affixed by screws proximally and distally. The ulna was intact but its distal end was resected to permit a more accurate repositioning of the fragments of the radius and to correct the radial deviation of the hand and wrist.

The illustrations of the anteroposterior and lateral roentgenograms made 3 months postoperatively show good incorporation of the iliac graft into the host bone. Note that while the density of the graft and radial fragments is the same, the ground glass-like appearance of iliac bone has not been lost at this time and the reformation of a medullary canal is not yet manifest roentgenographically.

for this complication always exists in this type of battle injury even with the best preparation and technique), the presence of foreign bodies will serve to encourage and perpetuate such an infection.

The technique of the plate-graft procedure has been described at length in the authors' original communication. They have found it of considerable advantage to utilize the electric knife and cautery in exposing the fracture and preparing the field for the graft and they have used this technique in exposing and removing grafts from the ilium. Both fields are kept dry by the use of continuous suction.

Although the soft tissues which have been dissected from both tables of the ilium are resutured with care, following removal of graft material, and despite hemostasis by the electric coagulator and the use of bone wax to control bone bleeding, ecchymosis and, in some cases, hematoma-formation may occur. The latter has been controlled without any ill-effect by early aspiration. The writers, who have attempted a second removal of bone from the same ilium in 2 cases and encountered considerable difficulty due to scarring and soft tissue adherence at the site of the bony defect. caution against this procedure and advise the use of the opposite ilium instead. These findings may account for the lack of residual disability following the resection of even massive portions from one or both iliums. There has been no instance of herniation through the iliac wound. The ilium at the site of resection will tend to regenerate, although defects are seen to persist in late postoperative roentgenograms.

Femur cases are brought to the operating room in their traction-suspension and are operated upon with the weight applied continuously to the pin through the distal end of the femur or the proximal end of the tibia. In the instance of other long bones a plaster-of-Paris support is applied several days before surgery and is bivalved to permit immediate application postoperatively, and this external fixation is usually changed 3 weeks postoperatively. The positioning of the patient at the time of surgery will depend entirely on the site of approach selected for the involved bone and depending on this position either the right or left ilium is used. For this reason *both* iliac crests are prepared preoperatively.

When necessary the patient is prepared with whole blood transfusions preoperatively and in all cases blood is administered during the operation. Usually 1,000 cubic centimeters is administered to femur and humerus cases and 500 cubic centimeters in operations on other long bones which permit the use of a tourniquet. The procedure can be greatly hastened by the use of two teams. In the last 5 months of this study the senior author found it necessary to prepare the field for the graft and to remove the graft himself. Despite this, the procedure has not become complicated and operation upon some of the most difficult femur cases has not exceeded 2½ hours. With a two-team technique the operation on the femur has been completed well within a 2 hour period.

Penicillin has been employed systemically in all cases, in doses of 20,000 units every 3 hours and, more recently, in doses of 40,000 units every 4 hours. Administration is begun at 6 p.m. on the evening before surgery and is

continued for a minimum of 5 days and in cases requiring extensive surgery for 10 days postoperatively.

As originally described in the instance of the femur, this long bone is exposed and a six screw plate is applied on the side of greatest stress, which is usually lateral as manifested by the tendency for lateral bowing in most instances. It is essential that a plate of adequate length be employed with a minimum of two screws above and two screws below the fracture level, which screws must include both cortices of the host bone. The authors have employed washers, fashioned from metallic plates, where it has been necessary to remove the hard outer table in reshaping the iliac graft and to assure a more adequate purchase of the screws. All metallic bodies have been constructed of stainless steel. Prior to the application of the graft, a trough is constructed and the medullary cavities of both fracture fragments are opened. This is done anteriorly or laterally depending on which side the plate has been applied. This cavity is filled with long strips of iliac bone and the massive iliac graft is then applied across this area and is fixed with one or two screws above and below the fracture level. It has been found advantageous to recess and to countersink this massive graft, for this assures more adequate contact with the host bone and, what is very important in cases in which there has been considerable scarring, facilitates closure of the overlying tissues without tension. Prior to the application of the graft the ends of the fragments may be drilled. Long slivers of iliac bone are placed across the exposed surfaces of the fracture. Except where it is necessary to remove tissue for exposure and graft application, the scar between the fragment ends is not resected and the fragments are not unduly exposed.

It was the authors' experience very early in the surgery of ununited battle fractures that the presence of marked scarring created difficulty not only in exposure but also in closure. Any attempt to close these wounds under tension may result in breaking down of soft tissues or create a dead space which encourages hematoma formation and the danger of secondary infection. It was also obvious that if an effort was made to expose the fragments freely and to attempt to correct overriding or bowing deformities, closure became difficult or impossible. For this reason, except in a few instances where the fragment ends have been widely separated, the usual procedure has been to disturb the position of the fragments very little or not at all and to expose them just sufficiently to permit application of the plate and countersunk graft, provided, of course that the general alinement of the axes of the fragments has been satisfactory.

Fig. 9. Compound comminuted fracture of the tibia, incurred in battle, with residual nonunion and a gap-defect of 3 inches (7.5 cms.). Operation was performed 6 months following the cessation of all drainage and after preliminary scar excision and the gap was bridged by a massive, full thickness iliac graft. The fibula was intact and a metallic plate was not applied. The illustration shows the roentgenographic appearance of the iliac graft 5 months postoperatively. Clinically the leg was quite stable. At the time that this report was completed, the extremity was protected in an ischial weight-bearing brace with a molded leather cuff for the leg.

Where the graft is employed without plate fixation, it is adequately shaped and is fixed with two screws above and two below the fracture level. The manner of fixation of the graft will vary depending on the mechanical requirements in each case, and this must be anticipated from the roentgenograms preoperatively and determined accurately at the operating table. It is preferred to apply grafts on the most vascular side, that is, away from scar and on the side most heavily muscled.

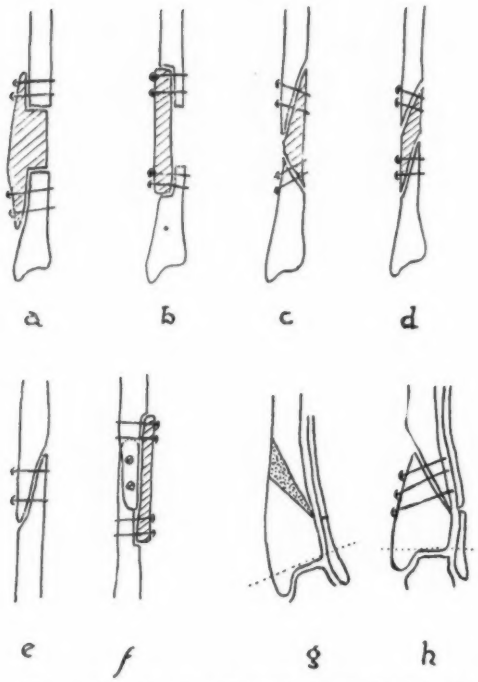


Fig. 10. Line drawings illustrating methods of shaping grafts for nonunion with defects in single forearm bones or in the tibia. a, Flange graft. b, Graft step-cut and recessed at each end. c, d, Trapezoid and parallelogram-shaped grafts to fit oblique ends of fracture fragments.

e and f, Fixation of the long oblique type of ununited fracture by multiple transfixion screws, with application of the bone graft at right angles to the direction of these screws.

g and h, Valgus deformity of the ankle and foot following malunion at the distal end of the tibia. Resection of a wedge, shaped so as to create, in effect, an oblique type of fracture which is fixed with several screws. The concept of this type of osteotomy is based on the success following multiple-screw fixation in the treatment of the acute type of long oblique fracture when open reduction is indicated, as well as in the treatment of similarly shaped ununited fractures as illustrated in e and f.

In the instance of a nonunion at the distal end of the radius, it has usually been found advisable, for adequate purchase of the graft, to bridge both nonunion and the wrist joint simultaneously and thereby to effect both healing of the ununited fracture and wrist fusion. In one instance of ununited fracture of the radius and another in the femur, the distal fragments were so severely porotic that a good purchase of the graft could not have been secured with screws, and the grafts were driven into and thoroughly impacted within the distal fragments.

The flange graft, devised by the authors for the filling of defects particularly of forearm bones, is shaped from the crest of the ilium in such a way that its body accurately fits into and fills defects up to 5 centimeters in length while its ends are shaped into flanges of about 2.5 centimeters in length for lateral application to the fracture fragments with screws above and below the gap-defect. Another type of iliac graft employed to fill large defects includes one table (for forearm bones) or both tables (for the tibia) and is applied by step-cutting its ends and mortising these into recessions at the ends of the fracture fragments where they are fixed with screws. A trapezoid-shaped graft or a parallelogram-shaped graft is best suited to fill a defect where the fragment ends are oblique (Fig. 10, a, b, c, and d).

Rigid fixation has been satisfactorily obtained in long oblique fractures by the use of 2 or 3 transfixion screws across the oblique fracture after baring the ends and reshaping them for accurate contact, and the graft is applied at right angles to these screws (Fig. 10, e and f). This technique has been employed in 5 cases, 3 times in the ulna and twice in the tibia with excellent union in all instances. In association with this experience, a method of osteotomy has been developed for the treatment of malunited fractures of long bones wherein a wedge of bone is excised in such a manner that not only is the existing deformity corrected but also a long oblique type of fracture is created which is held securely by two or three transfixion screws (Fig. 10 g and h). This procedure has been successfully performed on 6 patients, 3 in the tibia, 2 in the radius, and 1 in the ulna.

The usual approaches, that is, lateral and posterolateral for the femur, anterolateral for the humerus, posterior for the forearm (performed best with the arm across the chest) and anteromedial or anterior for the tibia, have had to be varied in some of these cases. It is presupposed that every effort will be made to replace inadequate skin through plastic surgery prior to the bone graft. This is essential especially if the approach must be made through or close to such an area, and also to

insure adequate nutrition of the fracture and the graft. The unfortunate fact, however, is that soft tissue scarring is often so severe that even such replacement of skin and subcutaneous tissue does not eliminate the massive scarring of the deeper tissues which may extend down to the bone itself. In such cases it has been advantageous to approach the long bone through more normal tissue and thus to completely avoid the severely scarred area. For example, an anterolateral approach to the tibia has permitted good exposure of the lateral aspect of the tibia and application of the graft on that side, while in one instance in the upper third of the leg, it has permitted the additional medial shifting of the fibula and its transfixion to the tibia. In two tibial cases, presenting severe anterior scarring despite previous pedicle skin grafts, a posterolateral approach was employed and the grafts were applied to the posterior surface of the tibia. However, exposure was found to be very limited and in one case the graft could be transfixed with only one screw above and one below the fracture level while in the other case the graft was placed in the prepared site across the fracture without screw fixation. It is, therefore, an approach that is not recommended as routine procedure but which may serve to advantage in this type of case.

4. Incidence and factors involved in failure of the graft operation—an evaluation of results up to March 15, 1946. A total of 91 bone graft operations have been performed on 85 patients. Of these, 34 have been by the combined plate-graft technique and include 31 operated on with plate and cancellous bone graft, 2 with plate and cortical graft (both in femurs with massive defects and nonunion), and 1 case with an ununited fracture of the neck of the femur in which the cortical grafts were combined with fixation by a Smith-Petersen nail. The site of operation was as follows: shaft of the femur in 22, neck of the femur in 1, radius and ulna in 5, humerus in 3, and tibia and fibula in 3. In 57 operations grafts were used alone with simple screw fixation and of these 54 had iliac grafts, 1 femur case with massive defect had combined cancellous and cortical grafts, and 1 case with a gap-defect in the humerus had two cortical graft operations. The site of operation in this group of cases was as follows: tibia in 16, radius in 15, ulna in 12, femur in 7, humerus in 5, spine of the scapula in 1, and clavicle in 1.

Massive defects of bone complicated the ununited fractures and exaggerated the complexity of their reconstruction in 29 cases. The bones were involved as follows: femur in 10, radius in 8, tibia in 4, ulna in 4 and humerus in 3. On the other hand, bone grafts were employed in the treatment of massive defects which were bridged by a narrow bony strut in only 8 cases: 5 in the femur, 1 in the humerus, 1 in the tibia and 1 in the radius. Adequate time should be allowed to permit hypertrophy of the existing strut and the authors have been amazed how often patients listed as potential candidates for bone replacements have demonstrated, after observation for several months, sufficient bone reformation so as not to require surgical interference. Experience with reference to the incidence of postoperative infection following reconstructive bone surgery in battle casualties, which will be discussed later, further justifies this conservative attitude. Large defects in the upper end of the femur and humerus, where the effect of the lever action of the extremity may prove very vicious, warrant consideration for surgery earlier than those defects of long bones distal to these levels. One must be guided by the size of the original bony strut bridging the defect, the progress of its hypertrophy during the ensuing months, and whether or not the defect is protected by an intact adjacent bone as in the forearm and leg.

An analysis of the plate-graft group indicates that definite union occurred in 20 cases observed for 4 months postoperatively or longer, and definite nonunion recurred in 2. One nonunion recurred as the result of faulty technique and has since been reoperated upon, while the other followed a postoperative infection. Satisfactory union was progressing in 8 cases observed over 10 weeks postoperatively, in whom the extremities were still protected in braces or casts, while in 4 cases, all femurs, it was too early to evaluate the probable end-results at the time that this analysis was completed. In 3 of these the postopera-

TABLE I.—RESULTS OF 91 BONE GRAFT OPERATIONS IN 85 PATIENTS

Performed between September 1, 1944 and March 1, 1946 and evaluated up to March 15, 1946

	No. of operations	Type of graft	Bones involved	Union following initial graft	Union following reoperation	Total union	Failure due to infection	Too recent to evaluate
Plate-graft technique	34	Iliac 31 Cortical 3	Femur 22 neck 1 Radius and ulna 5 Humerus 3 Tibia and fibula 3	28	1	29	1	4
Graft with screw fixation	57	Iliac 54 Iliac and cortical 1 Cortical 2	Tibia 10 Radius 15 Ulna 12 Femur (union in 5) 7 Humerus 5 Spine of scapula 1 Clavicle 1	45	5	50	2	5

tive course has been most satisfactory, while in one case the presence of a very mild postoperative infection left the fate of the graft in doubt (Table I).

In the patients treated by grafting without plate fixation 28 fractures were definitely united 4 months or more postoperatively, while in 6 patients there was definite recurrence of nonunion. Four of the recurrences were the result of errors in technique and were subsequently reoperated upon, and two recurrences followed postoperative infections. A fracture of the bony strut in another patient following a bone replacement operation for massive femoral defect, necessitated a second bone graft. Union had progressed satisfactorily in 17 cases observed for more than 10 weeks postoperatively, while it was too early to determine the course in 5 cases observed for less than 10 weeks at the time of this final analysis. In only one of these, because of a mild postoperative infection, was there any doubt as to the fate of the bone graft (Table I).

In the 8 cases of massive defects with union, replacement surgery was by massive iliac grafts alone. In one of these, a defect in the upper third of the femur, a fracture occured through the narrow bony strut, although the patient was still in suspension. He was reoperated upon by the combined plate-graft technique, and this instance served to impress the authors with the wisdom of utilizing plate fixation in addition to bone replacement in the treatment of massive defects, even in the presence of some union, in the upper end of the femur and humerus.

The authors can speak with certainty of an incidence of 9 failures of initial bone grafts by their technique, while in 2 other cases, both of whom had mild postoperative infections and had been observed less than 10 weeks, the fate of the graft could not be accurately determined at the time that this study was completed. Of the 9 definite failures, 3 were incidental to postoperative infections which required the removal of plate and graft, while 6 were the result of faulty technique. Five of these 6 cases, who had had cancellous grafts, were reoperated upon and progressed or were progressing to satisfactory union. In 4 of these patients the recurrences were due to failure to use a plate along with the graft. One was a nonunion of both bones of the forearm, another a nonunion of the surgical neck of the humerus, and the third and fourth were defects in the upper half of the femur. In a fifth case, with ununited fractures of both

bones of the forearm, the plate-graft technique had been used but the plate had been too short and had not bridged the gap-defect satisfactorily. The one cortical graft failure was the case previously referred to, with a massive defect in the upper end of the humerus and absence of the humeral head and glenoid, in whom a fibular graft had been initially employed with gradual resorption at its center and in whom at reoperation a tibial graft was applied across the fibular fragments (Fig. 4). The authors suggest that a fibular graft so used should not have multiple drill holes placed in its central portion, as recommended to enhance its revascularization, for they feel that this may encourage resorption and fracture in this region. They also feel that this hazard may be lessened by the additional use of slivers of iliac bones, placed along the surface of the cortical graft.

The authors feel that the end-results in the last 9 cases, performed during January and February 1946, could not be evaluated accurately at the time of this report. There have been, therefore, 9 failures following 82 initial bone graft operations in a series of 76 patients who have been observed a sufficient length of time, varying from 10 weeks to 18 months, and this represents an incidence of 10.8 per cent. Six of these 9 failures have been successfully reoperated upon—a total of 79 successful unions and 3 failures, as evaluated up to March 15, 1946 (Table I).

It has been experienced widely that the use of a plate for internal fixation of long bone fractures, particularly of the transverse type, will encourage delayed union and even nonunion, since the plate tends to hold the fragments apart and appears to discourage callus formation on the side to which it is applied. Six cases in this series were simple fractures of the femur which had been treated early by open reduction and plate fixation, and the occurrence of nonunion in these cases was unquestionably influenced by the use of these plates. The performance of iliac bone graft operations was greatly facilitated in these instances by the fact that the plate had already been applied and the bone fragments were well positioned, and since the fractures had been simple, dissection was performed with ease along anatomical planes. Union occurred in all six cases, and was sufficiently firm in one instance, 5 months postoperatively, to permit full weight bearing. The authors feel very strongly that the plate-graft technique will find eminent success in its use in ununited fractures in civil practice where many of the fractures have been simple and those that are compound present few of the complexities of battle fractures. They feel that the vicious features of plating as employed in the internal fixation of acute fractures do not apply in the combined plate-graft technique and that the only dangers involved are those incidental to the introduction of an inert metallic substance. The value of rigid fixation in the successful grafting of complicated ununited fractures of long bones as herein reported more than justifies the continued use of metallic plates and screws.

5. *Incidence and factors involved in the occurrence of postoperative infection; fate of iliac grafts in the presence of infection.* The authors have elected to wait at least 6 months following the cessation of all drainage before attempting any reconstructive bone surgery. This period represents a longer waiting interval than that accepted by other orthopedic surgeons, but the authors believe that the hazards of postoperative infection and of failure of bone grafting are exaggerated by such haste and the question in their minds at this time is whether a 6 months' waiting period is sufficiently long.

In this series, postoperative infections occurred in 11 out of 91 operations or 12.1 per cent. The local infection was moderately severe in only 1 case, requiring removal of the plate and graft 2 weeks postoperatively, and it was mild or moderate in the remaining 10 cases. Surgical interference could be safely deferred in these 10 cases for 4 to 6 weeks or more postoperatively, with control by penicillin and early drainage, without hazard to the patient. Six of these 10 patients have been operated on and plates and screws removed in 3 (2 femurs, 1 tibia) and the screws alone in the remainder (2 radii, 1 ulna). Two others, both femurs, were well united but persisting drainage 4 months postoperatively in both indicated the need for subsequent removal of

plates and screws. In 2 others, a femur and a tibia, the postoperative period of 8 weeks was considered too short for proper evaluation of the ultimate fate of the graft and removal of the metallic bodies had been deferred.

In 6 of the mild or moderately infected cases, 4 ununited fractures of the femur, 1 of the radius and 1 of the tibia, union occurred with incorporation of the major portion of the graft. Failure of union occurred in 2 more, both of whom originally demonstrated large gaps, but the graft became incorporated into one of the fracture fragments. In other words, where the infection had been mild enough to warrant delay in surgical interference (in 10 of the 11 cases), the graft became incorporated with union in 6 and became incorporated but with recurrence of nonunion in 2 more. The fate of the graft was in doubt in the remaining 2 cases at the time that this study was completed.

Definite failure of union following iliac bone grafting occurred in 3 cases in this entire series as a result of infection *per se*. *Postoperative infection, therefore, although a most undesirable complication, does not mean failure of an iliac bone graft if surgical interference can be sufficiently delayed.* The authors believe that this is more apt to occur with iliac bone as graft material because this type of graft is so rapidly invaded by new bone and incorporated into the host bone.

One cannot deny that once infection has occurred the metallic bodies employed for internal fixation, although inert, act by their presence to perpetuate the infection, and this applies whether stainless steel plates and screws or just screws alone have been employed. The only patient in whom the infection subsided spontaneously had had an iliac bone graft to fill a large defect in the tibia and this graft had been firmly mortised into the defect without screw fixation.

Nevertheless, although the presence of metallic fixation presents this untoward feature, the advantage of plate fixation is striking even in this group of cases. Of the 6 cases wherein union occurred in the presence of infection, 4 were ununited fractures of the femur and had had the combined plate-graft operation. The plates served to maintain rigid fixation at the operative site and preserved the alinement of the bone fragments until union had occurred and the foreign bodies could be safely removed.

The authors believe that these postoperative infections are not the result of faulty technique and offer as proof the absence of infection of the donor wounds in any of their cases. The incidence of infection reported herein parallels that recorded in other military installations. These battle fractures have been severely compound, they have been associated often with considerable soft tissue damage, and drainage has persisted for variable periods prior to complete healing. This background, as well as the condition of the involved extremity at the time of surgery, i.e., altered circulation, skin and soft tissue scarring and bony deformity, influence and encourage the occurrence of postoperative complications. It must be emphasized that in all of the cases presenting postoperative infection in this series there had been previous infection and osteomyelitis (compound battle fractures with drainage) and that this complication did not occur in any previously uninfected case.

The authors call attention to a factor which has received little or no attention, viz., the existence of living organisms at the site of original injury even in the absence of drainage from 6 months to one year. Cultures were made at the time of bone graft surgery in a group of 18 cases. These cases had not drained for at least 6 months and had adequate penicillin and sulfonamide therapy following the initial injury and at the time of bone grafting. Also, the gross appearance of the field at the time of exposure was satisfactory, i.e., there were no areas of necrosis, no dead fragments and no evidence of any inflammatory process. Positive cultures were reported in 9 cases or 50 per cent! Those patients with negative reports had an uneventful convalescence. Of the 9 patients with positive wound cultures, one had been a simple fracture of the humerus with failure of union following open reduction and plating, while the 8 remaining cases had been compound fractures, and all 9 cases demonstrated definite wound reaction postoperatively. Redness and induration of the wound occurred in 2 cases for 1 to 2 weeks postopera-

tively and then subsided (Staphylococcus albus 1, Staphylococcus aureus 1), seepage persisted for 2 weeks in 1 case and then subsided completely (Micrococcus spheroides), while mild drainage occurred in 5, the wounds requiring dependent drainage several days postoperatively (Staphylococcus albus 2, Streptococcus hemolyticus 1, Staphylococcus aureus 1). There was no reaction of the donor wound in any of these cases. While this series is far too small to render significant percentages, it is important to realize *that there are battle fractures, requiring reconstructive surgery, which under present standards have been considered adequately prepared for such surgery, wherein living organisms have been cultured and that such cases have manifested uniformly definite local wound reactions and, in some instances, actual postoperative drainage.*

The incidence of positive cultures might very well be higher in series where a shorter period than 6 months has been arbitrarily accepted as a sufficient waiting period. How may extension of the waiting period beyond 6 months lessen this hazard? Two of the cases yielded positive growths after waiting periods of 9 months and 1 year respectively! While there is no means at this time to determine the presence of living bacteria at the site of intended surgery, either prior to or at the time of surgery, a positive culture will at least serve to put the surgeon on guard. Penicillin and sulfa-sensitivity tests may serve to guide him in the use of these or other agents. Because of the inability at this time to determine the presence of living bacteria prior to, or during, surgery or to protect against or to eliminate this factor effectively, the authors have concluded that there will continue to be an *irreducible minimum incidence* of postoperative infection following bone graft or other reconstructive surgery of battle fractures.

CONCLUSIONS

1. The principle forte for the use of iliac bone has been the fact that it is cancellous and therefore accessible to rapid revascularization, and that it is richly osteogenic. There is reason to believe that some of the iliac bone survives, in contrast to a cortical graft, and the remainder becomes rapidly invaded by new bone. Iliac bone grafts maintain a density on roentgenograms which is comparable to that of the host bone and the relationship does not change with time.

A point to be considered in the use of iliac bone is whether the cancellous ilium undergoes metaplasia to assume an architecture capable of sustaining the stresses and strains of weight bearing and muscle pull and what time element is involved. Roentgenograms appear to show evidence of such metaplasia beginning at about 12 weeks after implantation, while roentgenograms at 6 months and longer show the grafts to be practically indistinguishable from the adjacent cortical bone.

Resorption of iliac grafts has occurred as late as 4 or 5 months postoperatively, due possibly to incomplete metaplasia and structural weakness of the graft and the result of stress and strain upon an inadequately protected graft. This also occurs with cortical grafts and is one of the dominant reasons for the use of internal metallic fixation in conjunction with grafting procedures.

2. There are certain instances where cortical bone must be employed, for example, where grafts must be excessively long and in cases in which an absolutely straight, rigid segment of bone is required.

3. To assure absolutely rigid protection during the phase of graft incorporation, especially where large defects are being bridged, it is recommended that the plate-graft technique be employed in the surgery of nonunion and massive defects of single long bones as the femur and humerus and in the presence of nonunion of both bones of the forearm and leg. Where one of the bones of the forearm is intact and in the leg in the presence of an intact fibula, the graft alone, held with two or more screws above and below the level of the fracture, offers adequate fixation.

4. The technique of plate-graft application and of fixation of the graft when used alone without a plate, must be varied to meet the mechanical requirements in each case. Incisions may have to be varied depending on the degree and site of soft tissue scarring. The oblique type of fracture lends itself very well to simple transfixion with the use of multiple screws.

5. Failure of the bone graft operation with recurrence of nonunion, excluding those cases associated with postoperative infections, has been due to such errors in technique as failure to use a plate when specifically indicated and failure to use a plate of adequate length.

6. Postoperative infection does not mean failure of iliac graft incorporation, especially if the infection is mild and well controlled and removal of the metallic fixation can be deferred.

In an effort to account for this complication, the authors place much significance upon the fact that in a certain number of battle fractures active growths of bacteria have been cultured from the site of original wounding six months to one year following the cessation of all drainage. Since there is no way, at this time, to determine accurately the presence of living bacteria at the site of injury prior to or at the time of surgery or to eliminate this factor effectively, the authors have concluded that there will continue to be an irreducible minimum incidence of postoperative infection following bone graft or other reconstructive bone surgery of battle fractures.

COAGULATION THROMBI IN SEGMENTS OF ARTERY AND VEIN IN DOGS AND THE GENESIS OF THROMBOEMBOLISM

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SINCE the early experiments of William Hewson, it is known that blood remains liquid for a long period of time between ligatures in a vein segment. This phenomenon was further studied by Baumgarten. He found that when the double ligature is applied under antiseptic precautions and the wound heals aseptically, the included blood column remains liquid. On the other hand such experiments without antiseptic precautions resulted in coagulation, a fact which has been confirmed by Senftleben in Cohnheim's laboratory.

Our problem was to investigate whether tissue juice from vein of homologous and heterologous origin would coagulate the stagnant blood within a formed vessel segment *in vivo*. This study was of special interest because it has been claimed that the endothelial lining prevents coagulation. We studied further the effect of human placental thromboplastin (10) on the formation of coagulation thrombi. Our observation also yielded information about the adhesiveness and syneresis of a blood coagulum formed within arterial and venous vessel chambers *in vivo*. The experiments were performed in healthy young mongrel dogs.

Because of the basic nature of these investigations pertaining to the phenomenon of thrombus formation and more recent studies on the phenomenon of platelet agglutination a discussion of thrombosis and of thromboembolism becomes necessary.

EXPERIMENTS

Procedure. The carotid artery is dissected free for approximately 8 centimeters and occluded with rubber shod clamps first proximally, then distally. A 25 gauge needle is introduced at the proximal end, care being taken not to injure the artery more than necessary. Blood is withdrawn from the occluded vessel segment into a syringe and the volume noted. One-tenth cubic centimeter of tissue juice or thromboplastin is introduced into the vessel segment. The needle is removed, the proximal clamp is released to allow the segment to fill with blood and the vessel is clamped over the orifice made by the needle. After an incubation period of from 1 to 9 minutes, the vessel is excised immediately, and placed on filter paper. Both clamps are removed and the vessel is cut along its long axis. The formation of the coagulum is noted carefully. As a control, the coagulant agent is replaced by 0.1 cubic centimeter of saline and the above procedure followed.

Results. Figure 1 shows, in full size photograph, a resected vein segment containing the coagulation thrombus. The photograph illustrates that there is no adhesiveness of the thrombus to the vessel wall. Upon removing the clamps, the thrombus emerged freely, without mechanical or manual manipulation. A small amount of serosanguineous liquid was present, apparently exhibiting syneresis.

Figure 2, an artery segment (full size), has been opened along its long axis to illustrate syneresis of the thrombus. This phenomenon is especially evident if one compares the length of the vessel with the length of the thrombus. On both ends of the segment one also can observe marked areas which are due to staining of the filter paper with serosanguineous liquid.

Table I shows results in 6 vein segments, 5 of which resulted in thrombus formation with an incubation time of 5 minutes, whereas 1 with an incubation time of 3 minutes did not exhibit coagulation. Table II presents the effects of vein juice from dogs and chickens on the formation of coagulation thrombi. In 7

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TABLE I.—IN VIVO ACTION OF DOG VEIN JUICE ON COAGULATION OF BLOOD IN VEIN SEGMENTS OF DOGS

Dog Number	Jugular vein R=Right L=Left	Segment length mm.	Blood volume c.c.	Vein juice c.c.	Incubation time min.	Coagulation	Syneresis	Adhesiveness to vessel wall
916	R	56	0.9	0.2	3	o		
	L	56	0.9	0.2	5	+†	+	o
817	L	60	1.5	0.2	5	+†	+	o
	R	63	1.6	0.2	5	+†	+	o
827	L	63	1.6	0.2	5	+†	+	o
	R	62	1.6	0.2	5	+†	+	o

o=negative †=complete
+=positive

segments employing vein juice from dogs, 4 coagulated completely after 1.5 and 3 minutes, whereas partial coagulation was formed in 2 segments following 2 minutes and in 1 following 3 minutes incubation time. Partial coagulation is designated by a coagulum which is mixed with coagulable whole blood. This is readily differentiated from serosanguineous liquid as obtained by syneresis by (a) its color, (b) the fact that it coagulates on standing, (c) its consistency in that it does not exhibit complete blood gelation but rather fibrin threads with or without gel formation.

Vein juice from chickens was employed in 6 segments resulting in partial coagulation after 1 and 2 minutes and complete coagulation after 4 and 5 minutes.

From Tables I and II it also can be seen that there are relatively large volumes of the test material as compared to the blood volume used in the arteries. This relationship, however, does not necessarily influence the coagulation time as may be seen in Table II. In dogs 902 and 828 both blood volumes were large and both test materials amounted to 0.1 cubic centimeter of the blood volume, yet par-

TABLE II.—VEIN JUICE OF DOGS AND CHICKENS INDUCING COAGULATION THROMBI IN SEGMENTS OF CAROTID AND FEMORAL ARTERIES

Dog						Vein juice from					
Number	Sex M=Male F=Female	Weight lbs.	Artery C=Carotid F=Femoral R=Right L=Left	Segment		Dog c.c.	Chicken c.c.	Incubation time min.	Coagulation	Syneresis	Adhesiveness to vessel wall
				Length mm.	Blood volume c.c.						
828	M	42	L.C.	70	1.0	0.1		1.5	+†	+	o
902	M	52	L.C.	71	1.0	0.1		2	(+)		
923	F	30	L.F.	52	0.2	0.1		2	(+)		
862	F	33	L.C.	66	0.3	0.1		3	(+)		
926	M	31	L.F.	50	0.3	0.1		3	+†	+	o
897	F	33	L.C.	64	0.6	0.1		3	+†	+	o
878	F	30	L.C.	61	0.3	0.1		3	+†	+	o
822	M	37	R.F.	67	0.4		0.1	1	(+)		
814	M	56	R.F.	56	0.4		0.1	2	(+)		
840	F	35	L.C.	71	0.9		0.1	2	(+)		
922	M	35	L.F.	53	0.2		0.1	4	+†	+	o
827	F	50	L.C.	72	1.0		0.1	5	+†	+	o
36	M	48	L.C.	70	1.0		0.2	5	+†	+	o

+=positive †=complete
(+)=partial
o=negative

Fig. 1. Coagulation thrombus in vein segment.

Fig. 2. Coagulation thrombus in artery segment.

tial coagulation was observed after 2 minutes in dog 902 and complete coagulation was found after 1.5 minutes in dog 828. Similarly in dog 922 with a blood volume of 0.2 cubic centimeter and 0.1 cubic centimeter of test material, coagulation was observed after 4 minutes. On the other hand with a blood volume of 0.9 cubic centimeter and 0.1 cubic centimeter test material, partial coagulation was found after 2 minutes in dog 840.

In comparing Tables I and II no conclusion can be made whether or not coagulation is enhanced in arterial or in venous segments. Only in 1 instance, in a vein segment of dog 916, was the incubation time found to be less than 5 minutes.

Table III lists the controls, physiologic saline being used in 6 artery and 4 vein segments. No coagulation occurred in the controls after 5 to 9 minutes incubation time.

The effect of Copley's preparation of purified thromboplastin from human placenta (10) upon coagulation thrombi is summarized in Table IV. Eight carotid arteries, 5 femoral arteries, and 16 jugular veins were employed. Coagulation occurred in all instances, except in 1 jugular vein segment with an incubation time of 1 minute. Another such segment of uniform length, blood volume, and amount of thromboplastin exhibited coagulation following the same incubation time. All coagulation thrombi exhibited syneresis and no adhesiveness to the vessel wall. It should be noted that in all cases the coagulation was complete.

Of interest is the comparison between length of the vessel segment and its blood volume. Vessel segments of 45 to 72 millimeters in length were used.

In all our observations on coagulation thrombi syneresis was always found even though the incubation time of the test material with whole blood was as short as 1 minute. From this one may infer that syneresis occurs rather immediately following coagulation within a vessel segment. Adhesiveness to the vessel wall was absent in all artery and vein segments in which coagulation thrombi had formed (Tables I, II, and IV).

Table V shows the results of several manipulations on the blood vessel, such as clamping it along the entire segment, applying a double silk ligature, insertion of a needle into the lumen, pinching with forceps along the entire segment, and crushing over silk with a hemostat. In 9 artery segments clamping with a hemostat after an incubation time of 5 to 8 minutes did not result in coagulation. In dog 924 the jugular vein was isolated for approximately 5 centimeters and ligated at its distal and proximal ends. This segment containing the column of blood was incubated for 18

TABLE III.— INFLUENCE OF PHYSIOLOGIC SALINE UPON STAGNANT BLOOD IN ARTERY AND VEIN SEGMENTS OF DOGS

Dog number	Blood vessel R=Right L=Left A=Artery V=Vein	Segment		0.9% salt solution cc.	Incubation time minutes	Coagulation
		Length mm.	Blood volume			
822	R. carotid a.	60	0.5	0.1	5	0
923	R. femoral a.	58	0.3	0.1	5	0
828	R. femoral a.	70	0.5	0.1	5	0
926	L. Carotid a.	61	0.3	0.1	7	0
814	L. femoral a.	60	0.5	0.1	8	0
929	L. femoral a.	61	0.4	0.1	9	0
851	R. jugular v.	60	1.2	0.2	5	0
851	L. jugular v.	60	1.2	0.2	5	0
873	R. jugular v.	58	1.6	0.2	5	0
873	L. jugular v.	60	1.7	0.2	5	0

0=negative

TABLE IV.— THE EFFECT OF PURIFIED THROMBOPLASTIN FROM HUMAN PLACENTA UPON THE COAGULATION OF BLOOD IN VIVO IN ARTERY AND VEIN SEGMENTS OF DOGS

Artery and vein segments				Thrombo-plastin c.c.	Incubation time min.	Coagulation	Syneresis	Adhesive-ness to vessel wall
Vessel	Total number	Length mm.	Blood volume c.c.					
Carotid artery	1	68	0.6	0.1	1	+†	+	o
	1	70	1.0	0.1	1.5	+†	+	o
	3	61–72	0.7–0.9	0.1	2	+†	+	o
	3	45–70	0.6–1.0	0.2	5	+†	+	o
Femoral artery	4	52–65	0.3–0.4	0.1	1	+†	+	o
	1	70	0.8	0.4	5	+†	+	o
Jugular vein	1	59	1.0	0.1	1	o		
	1	60	1.0	0.1	1	+†	+	o
	9	56–64	0.9–1.0	0.1	2	+†	+	o
	2	57–67	1.4–1.0	0.1	3	+†	+	o
	3	60–65	1.2–1.7	0.2	5	+†	+	o

†=complete
o=negative
+=positive

hours, during which time its coagulable blood did not coagulate. In 2 vein segments a needle was inserted with a stylet in place, and allowed to incubate in the stagnant blood column for 5 minutes. After this period of time the blood was not coagulated. In 2 vein segments, the blood was milked out of the segment manually and the vein crushed with a hemostat along the entire segment. The proximal clamp was then released to permit the vessel chamber to fill with blood. After an incubation time of 10 minutes, no coagulation occurred.

Upon longitudinal section of the vein segment, definite areas of injury to the intima were observed macroscopically. The same effect was also obtained in 6 out of 8 vein segments which were crushed over silk, according to the procedure of Murray (20). The incubation times were 10 minutes in 3 cases; 3, 30, and 36 hours in each one case with no coagulant effect. However, in 2 cases, in which incubation times were 24 and 48 hours, coagulation occurred and syneresis and nonadherence of the coagulation thrombi were found.

DISCUSSION

1. *Physical properties of coagulation thrombi.* Our observations are of fundamental significance, since they give evidence that a blood coagulum which is produced intra-arterially or intravenously without infection is a coagulation thrombus which is not adherent to the vessel wall and moreover exhibits syneresis (clot retraction). These latter phenomena, nonadherence and syneresis of a noninfected coagulation thrombus, together with clot firmness are the basis for the thromboembolic disease. It stands to reason that a clot that does not fill a vessel segment completely because of syneresis and which is not otherwise adherent to the vessel wall is likely to become an embolus. Recently the differentiation between phlebothrombosis and thrombophlebitis has been stressed by several surgeons, especially by Ochsner and DeBakey. In phlebothrombosis or the so-called quiet venous thrombosis of Homans a soft nonobstructing clot exists which increases the danger of embolism. In thrombophlebitis, on the other hand, the clot has been found usually firmly adherent to the vein wall and is therefore less likely to become detached and result in embolism. This contention, as far as the noninfected vessel wall is concerned, can be supported by our findings. We have not made any observations on the adherence and syneresis in infected vessel segments. Moreover, we found this phenomenon was present not only in vein segments but also in arteries.

TABLE V.— THE EFFECT OF CLAMPING, DOUBLE LIGATURE AND INJURY UPON BLOOD COAGULATION IN ARTERIAL AND VENOUS VESSEL CHAMBERS IN DOGS

Dog Number	C=Carotid A F=Femoral A J=Jugular V R=Right, L=Left	Length of segment mm.	Treatment	Incubation time	Coagulation
36	LFA	65	Clamping	5 min.	o
828	LFA	70	Clamping	5 min.	o
840	LFA	61	Clamping	5 min.	o
814	LCA	60	Clamping	5 min.	o
923	LCA	65	Clamping	5 min.	o
822	LCA	64	Clamping	6 min.	o
926	RCA	63	Clamping	7 min.	o
929	RFA	58	Clamping	7 min.	o
872	RFA	40	Clamping	8 min.	o
924	RJV	51	Double silk ligature	18 hrs.	o
856	RJV	66	Needle inserted	5 min.	o
856	LJV	66	Needle inserted	5 min.	o
922	RJV	60	Pinched with forceps	10 min.	o
922	LJV	60	Pinched with forceps	10 min.	o
875	RJV	58	Crushed over silk	30 hrs.	o
875	LJV	50	Crushed over silk	10 min.	o
875	LFV	43	Crushed over silk	10 min.	o
46–3	RFV	43	Crushed over silk	10 min.	o
46–1	LJV	75	Crushed over silk	24 hrs.	+xx
875	RJV	81	Crushed over silk	48 hrs.	+xx
46–4	RJV	75	Crushed over silk	3 hrs.	o
46–2	LJV	62	Crushed over silk	36 hrs.	o

o=negative
+=positive
xx=syneresis and nonadherence

The firmness of coagulation thrombi has not been studied. However, there can be wide variations in firmness of coagula of human blood as has been shown by Lalich and Copley (18) with a special viscometer. No correlation has been found between firmness and retraction of a blood coagulum according to Copley (9).

Attempts have been made by Vigyazo to produce experimentally clotting in segments of varicose veins in man. The resulting thrombus was a red or coagulation thrombus which was not adherent to the vein wall. Some clot adherence was only found after several days following the production of the thrombus. This latter observation was already made in 1856 by Virchow. He found that blood coagula are free during the first time following their production. Only later with the onset of chemical and morphological changes, stickiness occurs between them and the surrounding tissue. Virchow observed this in apoplectic extravasates of all organs, in the clots of aneurysms, and in the occluding plugs of veins.

2. Injury to the vessel wall and thrombus formation. Baumgarten observed that the complete stasis of the blood in a vessel segment does not necessarily lead to thrombus formation. He found that no coagulation occurred even if the intima is damaged because of the ligation. His experiments were carried out in arteries and veins of dogs, rabbits, and guinea pigs under aseptic conditions. In our experiments we found thrombi only in 2 out of 8 cases of severe injury (crushing over silk) to the vessel wall. No thrombi developed in 5 other instances with less injury to the vessel

wall. Our investigations suggest that the incubation period following injury may affect the formation of a coagulation thrombus.

The results show that crushing over silk in stagnant blood columns does not always produce coagulation thrombi. With circulating blood, it has been shown by Murray and associates (19) that white thrombi occur at the site of the injured vessel wall. However, in earlier investigations Welch claimed that "it is possible to produce experimentally severe injury of the internal coats of blood vessels without any resulting thrombosis."

One may argue whether or not the lesion of the endothelial cells or a dysfunction of the cells, as it was assumed by Cohnheim in 1882, would result in thrombosis. Bizzozero observed that in causing slight damage to the inner surface of an arterial wall in small mammals a so-called white thrombus was formed which consisted almost entirely of blood platelets. Later in 1886 Eberth and Schimmelbusch found that in damaged blood vessels first a white thrombus occurs which is mainly a platelet thrombus which may contain white blood cells. Upon this primary formation of a thrombus a second so-called red thrombus forms which is coagulated whole blood. Best, Cowan, and MacLean found that when a shunt, composed of glass or cellophane tubing is inserted between an artery and a vein in anesthetized dogs, cats, monkeys, and rabbits, large white thrombi rapidly form, and in many cases completely obstruct the flow of blood. These thrombi usually grow downstream rather than upstream from the original focus. Subsequently, to the white thrombus a red thrombus forms. These observations made in artificial vessel segments concur with the classical observations.

In the injured vessel in which the flow of blood is not completely and primarily blocked, platelets will adhere to the injured vessel wall and form platelet or white thrombi. This process may be enhanced by the infusion of tissue juice through the lesion in the vessel wall, since Copley and Houlihan (12, 13) have shown that tissue juice does agglutinate platelets although purified thromboplastin does not. An admixture of tissue juice is apparently not necessary to form white thrombi according to the experiments of Best, Cowan, and MacLean in artificial glass and cellophane shunts. However, in injured blood vessels, tissue juice may well enhance the formation of white or mixed thrombi. This process may be further augmented in infected or edematous vessels because of the infusion of larger amounts of tissue juice.

More recently Chambers and Zweifach made the observation that the interendothelial cement is sticky and offers considerable surface on the inner lining of the endothelium to which formed particles adhere. Whether or not defects in this lining or deficiencies of this substance comprising the interendothelial material would influence the formation of coagulation thrombi and agglutination thrombi will have to be decided in future experimentation. It is possible that the cement substance may itself contain a platelet agglutinant factor.

3. *The nature of intravascular blood clotting.* Blood clotting can no longer be considered primarily as the coagulation of whole blood, because of the recent observations on the mechanism of platelet agglutination (12, 13). In the following schema developed by Copley (11) the phenomenon of blood clotting is presented in all its possible occurrences.

Blood clotting according to the point of view presented in the schema is a general term for either plasma coagulation, cell agglutination, and clotting in which both phenomena are mixed. As plasma coagulation is understood that the precipitation of fibrin is synonymous with blood coagulation. This process may ultimately terminate in gelation of the blood plasma or the fibrin respectively. In the schema gelation is shown to occur with or without preceding fibrin formation.

It is not the scope of this presentation to discuss the mechanisms of fibrin formation and gelation. The phenomenon of cell agglutination is subdivided into agglutination of platelets, red and white cells. The agglutination of white cells which is known to occur appears to be insignificant because of the small number of white cells in normal blood. White cells may be agglutinated with platelets *in vivo* forming the so-called white thrombi. In red cell agglutination, immunologic reactions are prevalent, however, red cells may aggluti-

BLOOD CLOTTING

I. Plasma coagulation
  A. Fibrin precipitation
  B. Gelation
    1. With preceding fibrin formation
    2. Without preceding fibrin formation
II. Mixed (I and III)
III. Cell agglutination
  A. Platelet agglutination
    1. Without preceding fibrin formation
      a. Without subsequent fibrin formation
      b. With subsequent fibrin formation
    2. Immunologic?
  B. White cell agglutination
    1. With platelet agglutination, red cell agglutination
    2. Without platelet agglutination, red cell agglutination
  C. Red cell agglutination
    1. Immunologic
    2. With preceding fibrin formation

nate with preceding fibrin formation, as it is known in polycythemia vera. Platelet agglutination occurs without preceding fibrin formation and appears with or without subsequent fibrin formation. Whether or not immunologic reactions take place in the agglutination of platelets will have to be decided in future investigations. From this schema it is furthermore proposed to define thrombosis or thrombus formation as intravascular blood clotting during life.

This schema helps us to understand the differentiation between coagulation thrombosis, as produced in our investigations, and the agglutination thrombosis or mixed thrombosis, as produced by Best, Murray, and associates, and earlier in the classical observations by a number of workers. The injured vessel segment does not readily produce coagulation thrombosis, because apparently in a noninfected blood vessel, not sufficient tissue juice containing thromboplastin would infuse into the segment, as to initiate, by its content of thromboplastin, blood coagulation. In infected and edematous vessel segments coagulation thrombosis may possibly occur in a stagnant vessel chamber because sufficient tissue juice containing enough thromboplastin could enter the chamber and produce coagulation. It should be emphasized that tissue juice is not identical with thromboplastin although the latter substance is one of the constituents of tissue juice.

It may be inferred that the generally accepted differentiation between infected and noninfected thrombosis does not suffice. For a more advanced approach of various problems pertaining to thrombosis including effective therapy one should keep in mind the presented differentiation given in the schema. This presentation does not claim to include all possible influences and factors on thrombus formation, however, it is meant to be a guide for a better understanding of the problem of thrombosis. The general contention that thrombus formation in itself constitutes solely a coagulation phenomenon is theoretically no longer tenable.

4. *The genesis of thromboembolism.* According to Bauer emboli occur within 24 to 48 hours after thrombus formation in veins. During this time, "the wall of the vein is as yet not involved in any way and the thrombus is anchored only." This observation corroborates our findings that coagulation thrombi are not adherent to the vessel wall and are at the same time syneretic, both of which are of potential danger in the genesis of embolism.

The findings of Best, Cowan, and MacLean that white thrombi which are noninfected may break off easily appear to be of significance. Coagulation thrombi and agglutination thrombi may well become adherent to injured walls of infected blood vessels. The firmness of these thrombi under both infected and noninfected conditions will have to be investigated.

It should be emphasized that slowing of the blood stream, damage to the vascular endothelium, and changes in the blood must be regarded as causes of thrombosis. This view has been accepted by Aschoff in his latest publications on this subject (1, 2). Of interest are the observations of Copley, Krchma, and Whitney (14) who studied the anomalous flow proper-

ties of blood in viscometers. They found that heparin in increasing amounts tended to decrease the apparent viscosity, pseudoviscosity, and yield value of blood. These observations, when applied to the study of thrombosis, may establish still another factor contributing to the phenomenon of thrombus formation and possibly amplify the observation that retardation of the circulation is one of the main factors to promote thrombus formation.

The question of the prevention of the coagulation process for the prophylaxis and therapy of the thromboembolic disease by the use of anticoagulants such as heparin, dicoumarol, may be brought in briefly at this point. The effect of dicoumarol on platelet agglutination has not been well investigated to our knowledge. Since Copley and Houlihan (12, 13) have shown that prothrombin contains a platelet-agglutinant factor, it will have to be determined whether hypoprothrombinemia induced by dicoumarol also lowers the platelet-agglutinability of such plasma (11a). It has been reported that heparin in large doses prevents the agglutination of platelets *in vitro*. This observation could not be corroborated by Copley and Houlihan (12, 13) who used isolated washed platelet suspensions from blood of humans, dogs, swine, and rabbits which were strongly agglutinated by plasma containing extremely high amounts of heparin.

The reports concerning the clinical observations on the use of heparin indicate its high value in the prevention of thromboembolism, and may appear contradictory to the findings of Copley and Houlihan. A tentative explanation for the clinical value of heparin may be given as follows: the white or platelet thrombus may form by itself embolism which clinically may be less significant and not detectable because of an apparently smaller size than the usual size of the red or coagulation thrombi. For this reason it may be more practical to counteract the growth of coagulation thrombi in using anticoagulants. In conditions in which platelet agglutination thrombi are responsible, anticoagulants *per se* may not be of therapeutic value. In such conditions antiplatelet agglutinant substances will have to be found which counteract the formation of platelet thrombi.

CONCLUSION

Our observations offer evidence that a coagulum which forms within a noninfected artery or vein is syneretic and nonadherent to the vessel wall. These two phenomena are significant in that they are of potential danger for the genesis of thromboembolism.

SUMMARY

1. Coagulation thrombi were produced aseptically in 39 vein and 41 artery segments. The vessels used were the jugular and femoral veins and the carotid and femoral arteries of mongrel dogs.

2. Tissue juice of veins from dogs and chickens induced coagulation thrombi in arteries. Tissue juice from veins of dogs induced thrombi in veins.

3. Human placental thromboplastin, prepared according to the method of Copley, induced coagulation thrombi in arteries and veins.

4. All coagulation thrombi were nonadherent to the vessel wall and exhibited syneresis.

5. Physiologic saline, used as a control, did not cause coagulation thrombi.

6. Mechanical manipulations on the blood vessel, such as clamping, double silk ligature, insertion of a needle and pinching with forceps, did not produce intravascular coagulation.

7. Crushing of the vessel segment over silk produced coagulation thrombi in 2 out of 8 cases.

8. The nature of intravascular blood clotting and the genesis of thromboembolism are discussed.

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TRANSPLANTATION OF THE SPINAL CORD

The Problem of Kyphoscoliosis with Cord Signs

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UNCOMPLICATED scoliosis and kyphosis is not commonly associated with serious impairment of cord function. The term "uncomplicated" implies the exclusion of syringomyelia, intramedullary and extramedullary neoplasms and cysts. Fortunately, an uncomplicated kyphoscoliosis that develops slowly, even though quite severe, is seldom associated with paralysis of cord function. Likewise, kyphosis that results from tuberculous infection of the spine is uncommonly associated with paralysis of the lower extremities or loss of bowel and bladder control. Tuberculosis is the most common direct and known cause for kyphosis. At times the severity of the deformity and acute angulation of the spine would make it seem incredible that the cord could maintain its physiological integrity. The facts, however, demonstrate a notable faculty of nervous tissue—the faculty of adjusting to insidious changes in shape, compression, and stretch. The many cases of marked "hunch back" and "gibbus" that never suffer the deficits of cord paralysis draw attention to this remarkable property of nervous tissue.

However, when kyphoscoliosis is associated with serious cord impairment, a real and challenging problem is presented. Such patients usually turn up in orthopedic clinics and there is often much debate between orthopedist, neurologist, and neurological surgeon concerning the mechanism of cord impairment, what to do about it and how. At first, conservative treatment is usually tried and consists of some effort gradually to straighten the spine. I think it fair to say that the results of conservative treatment in such cases are usually failures. When surgery is proposed the usual routine considerations are: (1) What does one expect to find—a derangement or compression of the cord due to angulation of the spine or a coincidental neoplasm? (2) If the derangement is purely on a mechanical basis, can one expect a simple laminectomy to correct it?—probably not. (3) One cannot perform a laminectomy with impunity upon an already weakened and deforming spine; hence there should be reasonable hope of accomplishing some benefit.

For some years I had the opportunity of engaging some of these problems in the orthopedic clinic of Dr. Arthur Steindler in Iowa City, Iowa, and together we arrived at some convictions in respect to the tuberculous kyphosis with developing signs of cord compression.

Two years ago I did a laminectomy with some trepidation upon a boy with a marked kyphoscoliosis of unknown origin and recent paralysis below the waist. It seemed logical that the acute angulation in the cord could be relieved by widening the spinal canal, freeing the cord and moving it into a new bed. The result was most gratifying. It is felt, therefore, that the results of these experiences might serve to broaden the indications for surgery in such cases and to widen the scope of surgery in an attempt to salvage a patient otherwise doomed to cord paralysis.

LATERAL TRANSPLANTATION OF THE SPINAL CORD IN KYPHOSCOLIOSIS

G. S. (70660), a Mexican boy, age 16, was referred by the New Mexico Department of Public Welfare and admitted to the Presbyterian Hospital, Denver, Colorado, on December 4, 1943.

Three months ago while engaged in digging ditches for the railroad, he noted that he was dragging his feet. Paralysis of the lower extremities gradually developed to complete loss of voluntary control, and he had been confined to bed for the past 5 weeks. For the past 2 weeks he has had increasing difficulty in voluntarily emptying the bladder and bowel. About 3 years ago he noticed that his upper spine was "growing crooked." There was no past history that suggested tuberculosis or syringomyelia.

The boy was of normal size and weight for his age and except for the kyphoscoliosis and neurological

deficits described, the general and neurological examinations gave normal findings. There was total motor paralysis of both lower extremities except for the ability to move the left large toe slightly. The patellar and Achilles tendon reflexes were hyperactive. There was patellar and ankle clonus and the Babinski sign on both sides. All forms of sensation were lost up to the level of twelfth dorsal and partial loss of pain, temperature, and touch sensibilities for three segments higher. Routine examinations of the blood and urine gave normal results and the blood Kahn test was negative. Roentgenograms of the lungs revealed no evidence of tuberculosis. Films of the dorsal spine showed a marked scoliosis to the right with maximum angulation at the sixth dorsal (Fig. 1). There was no evidence of other pathology in the spine or ribs.

Fig. 1. A drawing made from a roentgenogram of the dorsal spine in the case of G. S. to illustrate the degree of scoliosis. The maximum angulation is at the sixth dorsal.

In view of the seriousness of the neurological findings, it was felt that an exploration of the spinal cord was advisable. On December 9, 1943, the laminal arches from the second dorsal to the seventh dorsal inclusive were removed under avertin anesthesia. No evidence of extradural cyst or neoplasm was disclosed. An incision was made in the dura and a soft rubber catheter was easily passed upward to the seventh cervical and downward to the twelfth dorsal. The cord, except for a marked rotation and angulation, appeared normal. There was no evidence of bone pathology within the limits of the exploration. It was concluded that the angulation of the cord had been exaggerated rather acutely, and that this was the factor responsible for loss of function. It being obvious that the laminectomy had not relieved the deformity, the idea of transplanting the cord seemed logical. To accomplish this, portions of the pedicles and transverse processes of the vertebrae and heads of the ribs at the fourth dorsal to the seventh dorsal inclusive were rongeured away on the concaved side. Four pairs of nerve roots were ligated and severed extradurally from the third to the sixth dorsal, inclusive. As soon as the roots were severed, the cord with very little aid assumed its new position so as to relieve the acute angulation (Fig. 2) The wound was closed in the usual manner without further procedure.

The postoperative course was uneventful except for a superficial infection in the wound which healed readily. Within 3 days the patient began to recover sensation and motor function in the lower extremities. On January 22, 1944 a plaster jacket was applied from shoulders to groins, and on March 17, 1944 he was discharged with almost complete recovery of sensation, motor function, and bowel and bladder control. He returned home by train and fully ambulatory.

A follow-up letter from the Public Welfare of New Mexico on March 9, 1946 (2 years following discharge from the hospital) stated that several check up examinations revealed a continued state of well-being. A recent check by Dr. R. E. Forbis, Hot Springs, New Mexico, revealed no losses in the neurological status, and the scoliosis appears to have become quiescent. (In May, 1944, a Taylor brace was substituted for the plaster jacket.) The boy is ambulatory without crutches and has been trained in boot making by the State Vocational Rehabilitation Service.

Cord signs associated with scoliosis of this type are rare. The impairment of cord function in this patient was undoubtedly due to a more rapid development of acute angulation than usual. The cause of the scoliosis is undetermined and no other pathology of the spine or cord could be demonstrated. The rapid recovery of function after the acute angulation of the cord was relieved and the patient's course during the past 2 years indicate that there is no other pathology in or about the cord. Laminectomy alone would have afforded no relief, but the results of the cord transplantation show the possibilities of extended

Fig. 2. A drawing to illustrate the manner in which the cord was transplanted in the case of G. S. After ligating and cutting the nerve roots extradurally from the third to the sixth dorsals inclusive, the cord was moved into its new position and the acute angulation relieved. The patient presented the neurological deficits of almost complete transverse lesion of the cord before operation. Full recovery was resumed following the operation and has been maintained to the time of writing (2 years).

surgery and pave the way toward a more rational solution of the problem.

THE PROBLEM OF THE TUBERCULOUS SPINE WITH CORD SIGNS

As already pointed out, significant cord impairment is not commonly associated with tuberculous kyphosis but occasionally the syndrome does occur. I had the privilege of studying and operating upon 3 such patients in the clinic of Dr. Arthur Steindler, and the conclusions and convictions that were evolved from the study are briefly as follows: (1) In all 3 cases a considerable mass of tuberculous granulation tissue was disclosed intraspinal and extradural. The mass of tissue compressed the cord and was the causal factor for the onset of paralysis. In 2 of the patients the kyphosis was of only moderate grade while in the third it was severe. All 3 patients had had tuberculosis of the spine for a long time, but the development of cord signs was relatively acute. The granulation tissue (containing some pus) was situated at the kyphotic angle, the locus of maximum intensity of the pathology of the spine. (2) The development of a tuberculous abscess or tuberculous granulation tissue intraspinal may occur at any time during the patient's course, depending upon the quiescence or activity of the lesion. (3) The progress of cord impairment will ordinarily be relatively rapid, measured in terms of days or weeks. (4) Laminectomy is indicated in such cases and should not be postponed unreasonably long. The granulation tissue and pus should be removed or adequately decompressed. Obviously the dura should not be opened. It is perhaps best not to drain the wound, but if a rubber drain is left in place, it should be removed in 24 hours. (5) The kyphosis is not the cause of cord impairment. One can be reasonably certain that an expanding mass is developing intraspinal which can and should be removed. As a matter of fact, these pathological events are well known, and there should be no puzzling equivocation in arriving at the diagnosis and logical treatment. It is a fact nevertheless that when confronted with a patient who has a severe kyphosis of long standing and thought to be quiescent and who begins to develop signs of cord paralysis, there may be considerable indecision relative to the indications for surgery.

The problem here is not unlike that of osteomyelitis of the spine associated with extradural abscess in respect to diagnosis and treatment. Paralysis develops in the course of days and unless the cord compression is relieved by laminectomy before paralysis is complete, the prognosis for return of function is notoriously poor. Spinal punctures are contraindicated in both the pyogenic and tuberculous infections.

TUBERCULOSIS KYPHOSIS WITH COMPLETE CORD LESION OF LONG STANDING (ANTERIOR TRANSPLANTATION OF THE CORD)

A. R., a white male, aged 41 years, was admitted to the Presbyterian Hospital, Denver, Colorado, on April 16, 1944. He complained of severe pain in the distribution of the eighth, ninth, and tenth dorsal nerves. He developed a tuberculosis kyphosis as a child and almost lost the use of his legs at the age of 14. He managed to get about with crutches until the age of 38 when he developed the signs of a complete transverse lesion at D-10.

Examination revealed complete sensory and motor paralysis up to the level of tenth dorsal and loss of

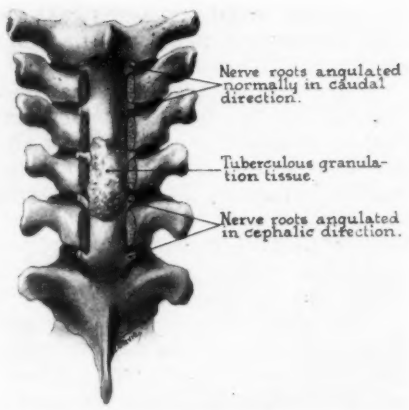
Nerve roots angulated normally in caudal direction.
Tuberculous granulation tissue.
Nerve roots angulated in cephalic direction.

Fig. 3. A drawing to illustrate the intraspinal findings in the case of A. R. After removing the laminal arches of the eighth to the eleventh dorsals inclusive a large tumor-like mass of fibrofatty tissue presented extradurally at the apex of the kyphotic angle. It had compressed the cord to about one-sixth its normal size. Note how the kyphosis and collapse of vertebral bodies cause a reversal of the normal angle which nerve roots make with the cord.

voluntary bowel and bladder control. There was a marked gibbus at ninth and tenth dorsal. A roentgenogram of the spine showed an extreme kyphosis with angulation at ninth and tenth dorsal and considerable destruction of these vertebrae. The findings were those of an old Pott's disease with no evidence of recent activity.

I had intended to attempt an alcohol injection of the involved nerves to relieve a traumatic neuritis, but this was abandoned because of the severe deformity and distortion of anatomical landmarks. A laminectomy was decided upon for the purpose of cutting the appropriate nerve roots intraspinally.

On May 1, 1944 the laminal arches from the eighth to the eleventh dorsal inclusive were removed. A thick mass of tough scar tissue presented at the ninth and tenth dorsal segments. It was situated posterior to the dura and compressed the cord to about one-sixth its normal size. The mass consisted of fibrofatty tissue, and in my opinion was obviously the end-result of tuberculous granulation tissue established in early life (Fig. 3.) The nerve roots from the seventh to the eleventh dorsal inclusive and on both sides were ligated and cut extradurally to alleviate pain. By gentle retraction of the cord to one side and then the other the posterior aspects of the vertebral bodies and intervertebral discs were chiseled

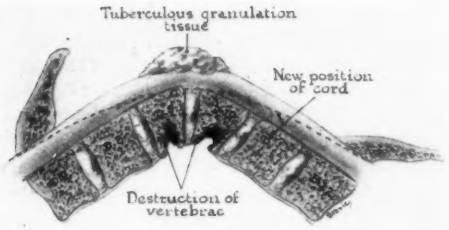

Fig. 4. A drawing to illustrate the manner in which the cord was transplanted anteriorly and the acute angulation relieved. The new position of the cord indicated by dotted lines is somewhat exaggerated in the drawing. The maximum shift in position anteriorly was one-quarter inch.

away in such a manner as to relax the acute angulation of the cord (Fig. 4). Recovery of function was not anticipated because of the long standing paralysis, but the feasibility and ease of anterior transplantation of the cord was demonstrated. There was no evidence of active pathology and the wound was closed in the usual manner.

The patient was considerably relieved of girdle pain but to the time of writing 22 months since the operation, there has been no evidence of return of cord function.

There is no question concerning the cause of the transverse myelitis in this case and had a laminectomy been performed early in life when the cord signs made their first appearance, this patient might well be ambulatory. This is the significant lesson to be drawn from the case. There appeared to be two episodes in the patient's history. At about the age of 14 he became partially paralyzed but managed to get about with the aid of crutches. At the age of 38 the paralysis became complete. Judging from the histology of the scar tissue, I do not believe there was a recrudescence of active tuberculous pathology. The intraspinal mass of tissue was established early in life and was of considerable size. It is quite likely that some small aggravation of the kyphosis at the age of 38 was sufficient in conjunction with the tumor-like mass to complete the transverse lesion of the cord.

EVALUATION OF RESULTS

In respect to the possibility of anterior transplantation of the cord, I feel the follow-

ing remarks are pertinent: (1) I do not feel that the procedure has an application of special importance in the treatment of tuberculous kyphosis with cord signs. The causal factor in these cases has already been elaborated. Moreover, in the treatment of active tuberculous infection more harm than good might easily be done in attempting such a procedure. (2) The application of anterior transplantation of the cord may be of value, however, in other types of cases; for example, in the case of rapidly developing acute kyphosis following trauma. (3) In performing a number of laminectomies in cases of compression fracture of the spine associated with a transverse cord lesion, I have been impressed with some consistent findings. It is often difficult to correlate the benign appearance of the cord at the level of the fracture with its total and permanent loss of function. Macroscopically and to palpation, at any rate, there often appears to be no anatomical disruption or softening of the cord. There is almost always, however, an acute hump, knuckle, or angulation in the cord due to a posterior protrusion of the fractured vertebral body. A simple laminectomy does not correct this deformity. I have strongly entertained the belief that the acute pressure of the bony protuberance that indents the anterior aspect of the cord impairs or obstructs the anterior spinal artery. It may be possible that the resulting vascular insufficiency contributes materially to the transverse myelitis and impairment of cord function. In any case, if an emergency laminectomy is performed in the case of acute spinal fracture with transverse myelitis, I feel the significant objective consists in removing the bony or cartilaginous protrusion into the spinal canal. While this is quite possible technically, it should be done with great care. Careless retraction of an acutely damaged cord would obviate all chance of recovery. If one or two pairs of neighboring nerve roots are ligated and cut extradurally, retraction of the cord and chiseling of the protruding vertebral body is greatly simplified. However, one hesitates to disturb ever so little the blood supply to the damaged cord segment by severing the arteries that accompany nerve roots. These factors must be left for future evaluation and should be determined for the individual case. While such treatment of the acute spinal fracture may not be strictly relevant to the concept of cord transplantation, it is discussed because the technical procedure is much the same as for the latter.

SUMMARY AND CONCLUSIONS

The feasibility and indications for lateral and anterior transplantation of the spinal cord are discussed. A case of severe kyphoscoliosis with acute angulation and physiological transverse lesion of the cord is presented. The cause of the scoliosis was undetermined. Lateral transplantation of the cord with relief of the acute angulation resulted in complete resumption of cord function.

The onset of serious cord impairment associated with tuberculous kyphosis should be considered due to an intraspinal tuberculous abscess or growth of granulation tissue. Laminectomy and decompression of the cord are definitely indicated. A case of tuberculous kyphosis with transverse myelitis of long standing is presented. A tumor-like mass of scar tissue was disclosed intraspinally at the apex of the kyphotic angle. This mass was the responsible factor for the complete transverse lesion of the cord and was the result of tuberculous granulation established early in life.

RECONSTRUCTIVE SURGERY OF THE CHEST WALL

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ALTHOUGH thoracic surgery is one of the newest fields of surgical development, the results achieved during the past two decades have been remarkable. Significant contributions to this field of surgery have been made by Lilienthal, Sauerbruch, Nissen, Churchill, Cutler, Graham, Alexander, Beck, Blalock, Rienhoff, and Blades. The advances made in reconstructive surgery of the chest wall, however, have not paralleled the advances made in intrathoracic surgery. Plastic or reconstructive surgery should, by no means, be limited to those parts of the body that are exposed. From the standpoint of plastic surgery, there is no essential difference between the repair of defects of the chest wall or the extirpation of a recurrent carcinoma of the chest wall following a radical mastectomy and the covering of an injured eyelid, the closure of a salivary fistula, the removal of a carcinoma or scar of the face, or the re-establishment of motion in a hand distorted as the result of burns. The textbooks on general surgery, however, devote little if any space to reparative surgery of the chest wall, although some operative procedures for the repair of defects in this region may be found in specialized articles (13, 16).

There are many conditions of the chest which may not respond well to ordinary procedures but which can be greatly benefited by the application of the more intensive and specialized techniques developed from experience in plastic surgery. The purpose of the present paper is the enumeration and brief description of certain of these conditions and a more detailed account of the procedures employed in the treatment of 3 specific conditions, namely, recurrent carcinoma of the breast, persistent bronchial fistulas, and hypertrophy of the breast.

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SURGICAL TREATMENT OF RECURRENT CARCINOMA OF THE BREAST

Few operations have been designed for the eradication of neoplastic processes recurring after the removal of tumors of the breast and chest wall either by surgery or by irradiation. The use of irradiation therapy to supplement surgical excision has prolonged the life of some patients with recurrent cancer of the breast, but many do not receive the benefit of irradiation when the disease has recurred, and only rarely is the surgeon willing to make a second attempt to eradicate the disease. The statements (3) that "recurrent or metastatic deposits of mammary cancer which make their appearance following radical mastectomy are manifestations of an incurable disease" and that "the disease cannot be eradicated in this stage by any of the therapeutic measures available at present" are, fortunately, no longer true. Any operation which improves the effectiveness of surgery or irradiation or which prolongs life must be considered of value.

The distinction between recurrent and metastatic cancer is seemingly an arbitrary one. The *recurrent* lesions are those which appear in areas which are easily accessible to operation. The *metastatic* ones appear in more distant organs. Geschickter has found that recurrence is seen in the skin and subcutaneous tissues of the chest wall, in the lymph nodes of the axilla or supraclavicular region on the affected side, and in the opposite breast, in this order of frequency. Nodules in the skin of the chest wall, in the parasternal region, are the most common type of skin recurrence following radical mastectomy. Other similar manifestations include recurrence in the scar, isolated nodules in the skin, multiple nodules of carcinoma *en cuirasse*, and the carcinomatous dermatitis referred to as inflammatory or erysipeloid cancer.

Major factors influencing the probability of recurrence and determining the technique for

eradication of the recurrent growth are the type of incision and procedure employed in the initial operation for mastectomy. Numerous modifications of the original Halsted (7) operation have been made by different operators (5, 10, 14, 17, 18) independently or inspired by Halsted's work (Fig. 1). Time and experience, however, have led the majority of surgeons to a fuller appreciation of Halsted's (6, 8) basic methods and principles. In using the elliptical incision which parallels the anterior axillary fold, the operator may follow either the Halsted or the Handley techniques. That of Halsted, which frequently necessitates grafting, requires the removal of a wide margin of skin around the growth. The Handley technique involves removal of less skin, but more extensive undermining of the flaps in order to secure primary closure. Stewart employs transverse elliptical incisions, which may permit the removal of large amounts of skin and primary closure without grafting (Fig. 1).

Whatever the type of radical mastectomy preferred by the surgeon, an attempt is made at operation to remove in one mass all of the structures which are liable to immediate invasion by the tumor. Because of the assumption that spread of the disease from its original focus proceeds by continuous permeation in all directions, an extremely wide excision *en bloc* of the structures surrounding the primary tumor is advisable. Separation of the tissues by any means within the operative field must be scrupulously avoided, for such separation may result in the invasion of structures by tumor being left behind. Halsted's original basis for the operation was empirical and antedated Handley's theory of lymphatic permeation by cancer cells. However, Halsted's experience with the localization of recurrences and metastatic foci following less extensive types of mastectomy is ample reason to attempt the widest possible excision.

It is true that in some cases the extension of the cancer occurs by way of the blood stream and that tumor emboli may result in distant metastases even though the microscopic examination of the specimen following radical mastectomy fails to show involvement of the axillary lymph nodes and neighboring tissues. Nevertheless, the operation originally conceived by Halsted (7) and Meyer remains the standard procedure for radical mastectomy since it is based on sound surgical and pathological principles and is applicable to the majority of cases in which clinical evidence fails to indicate that the disease has already passed beyond the scope of operability. The proximity of the cancer to vital structures and its extent at the time of operation greatly influence the success of treatment.

Geschickter states that the 5 year survival rate in surgery in operable cancer approximates 70 per cent for cases without axillary involvement and 25 per cent in cases with axillary involvement. The two groups are about equal in size. The combined curability averages 47 per cent. Adair found that the 5 year survival rate for radical mastectomy in the operable group was 45 per cent and only 18 per cent in a similar group treated by irradiation alone.

The criteria for inoperability should not influence the surgeon to exclude operation for palliative reasons, in cases in which irradiation is inadequate or contraindicated; nor should it be assumed that all of these patients are definitely incurable, as was the assumption in the cases here presented (Figs. 2, 6).

CASE 1. A 44 year old white woman was admitted to the Duke Hospital May 10, 1945. Ten years previously, a mass had developed in the left breast which was excised at another hospital. It promptly recurred and a radical mastectomy was performed by a second surgeon. During the ensuing year, she received intermittent irradiation therapy, following which she remained asymptomatic for 5 years, when the lesion recurred in the chest wall. A biopsy was taken and histologic sections disclosed a "recurrent medullary carcinoma." The lesion was considered "inoperable" and palliative irradiation was instituted. The patient was given a total of 2100 roentgen units to the primary recurrence with the use of 200 kilovolts, 30 centimeters' distance, 0.2 tin filter. Three months later, this same area was given 2,200 roentgen units with 200 kilovolts, 30 centimeters' distance, 0.5 copper filter, with the lesion well shielded. The patient returned 12 months later with numerous areas of recurrence in the skin of the chest wall each of which was treated separately by superficial x-ray therapy. She was also given 1200 roentgen units as a sterilization dose. The lesions subsided, but when they recurred 1 year later, she could not tolerate any additional irradiation, whereupon she was admitted to the hospital for operation. There was a large recurrent carcinoma of the left chest wall, with ulceration and secondary infection

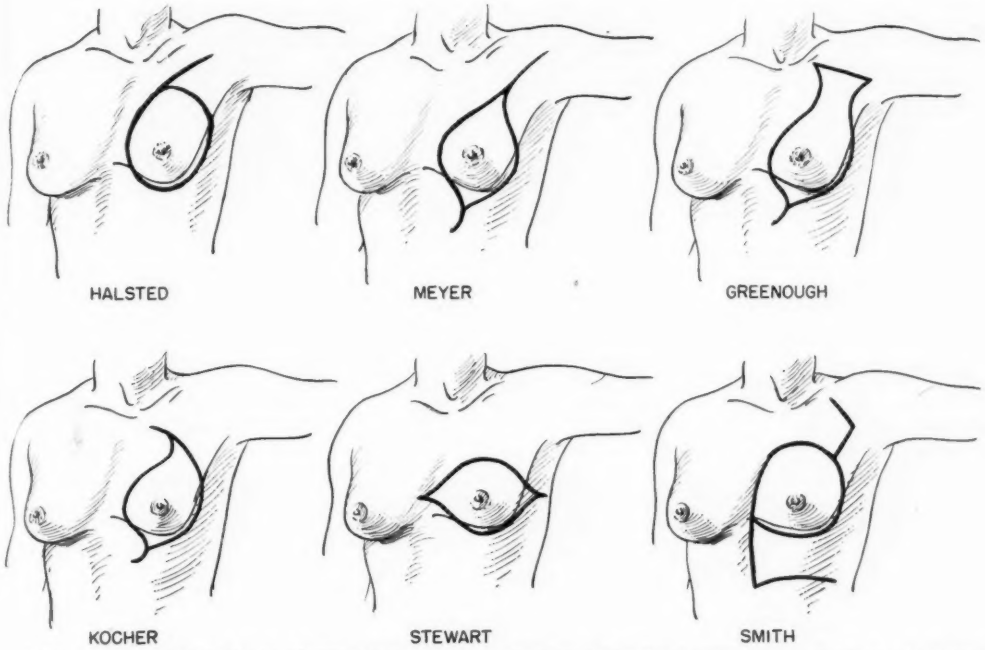


Fig. 1. The major factors which influence the probability of local recurrence are the type of incision and procedure employed in the original operation for mastectomy. Numerous modifications of the original Halsted incision have been made by different operators (5, 10, 14, 17, 18). Whatever the type of incision employed, an attempt should be made to remove *en bloc* all of the structures which are liable to immediate invasion by the tumor.

(Fig. 2a). An exposed rib could be seen at the base of the ulcer. The surrounding skin was thin and telangiectatic. Pain was constant and intractable.

Operation. Excision of recurrent carcinoma of the chest wall; application of split thickness skin grafts to pericardium. On May 12, 1945, with the patient anesthetized with sodium pentothal and nitrous oxide, a closed system being used, the entire chest, abdomen, and one thigh were prepared as a sterile field. The proposed area of excision was widely outlined by a toothpick moistened with 5 per cent alcoholic solution of brilliant green. The medial incision extended along the right lateral border of the sternum. The superior limb followed the clavicle high into the axilla (Fig. 3). The inferior incision began along the right costal margin and traversed the left costal margin. The lateral incision followed the medial margin of the latissimus dorsi. The recurrent carcinoma and the soft tissues of the entire left chest wall were removed *en bloc* beginning at the periphery. The tumor had invaded the underlying ribs; and parts of the sternum together with the third, fourth, fifth, sixth, and seventh ribs were resected, and the pericardium was exposed (Fig. 3). There were no visible implants in the pleura.

The very large operative defect was reduced somewhat in size by approximating the four corners (Fig. 5). It was impossible to cover the defect with a direct transfer flap or to utilize the right breast, which was quite small. There was no alternative other than to tack the pericardium to the intercostal muscles and sternum (Fig. 4), by interrupted sutures of white silk. Although the heart was seemingly lifted forward by this tacking procedure, there was no visible interference with its function. Two large heavy split thickness skin grafts cut from the thigh were sutured to cover the operative defect which measured 8 inches wide (17.6 cm.) and 9 inches long (19.8 cm.) (Fig. 5). The suture ends were not cut so that they could be tied over a bolus of cotton waste to obtain pressure on the graft, directly over the pericardium. The operative area was dressed 10 days later at which time there was an almost complete "take" of the graft, except for a 1 centimeter area over a protruding portion of a resected rib which did not completely heal for several weeks. The patient at present (Fig. 2b, c, d) is entirely well and performs her household duties without symptoms. She does not wear a protective support. The electrocardiogram is normal, and no murmurs are heard over the heart. There is no evidence of local recurrence or distant metastases.

The graft has remained soft and semitransparent. Cardiac contractions and pulsations are clearly visible. Forced expiration with increased intrapulmo-

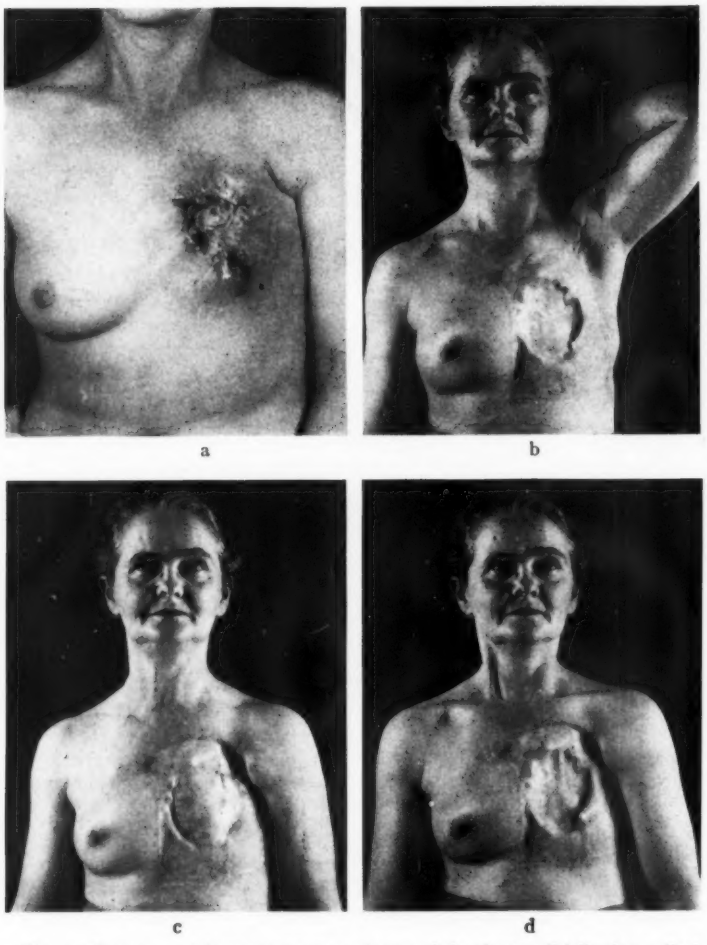


Fig. 2. Case 1. a, A large recurrent carcinoma of the chest wall following radical mastectomy and irradiation therapy. Her condition was thought to be inoperable. She could not tolerate additional irradiation. b, Lesion widely excised together with underlying ribs and sternum, and split skin grafts applied directly to pericardium and chest wall. c, Position of graft in forced expiration. d, Graft-covered pericardium is drawn inward at beginning of inspiration. Photographs b, c, d were taken 10 months following operation.

nary pressure causes the graft covered pericardium to bulge beyond the surrounding chest wall (Fig. 2c). When the patient decreases her intrapulmonary pressure, the graft covered pericardium is drawn inward below the level of the chest wall (Fig. 2d). Violent waves are seen when the patient coughs.

So far as we are aware, this is the first time that a skin graft has been applied directly to the pericardium.

Case 2. A 45 year old colored woman was first admitted to the Duke Hospital January 9, 1945. Five months previously, she noted a mass in the left breast which continued to increase progressively in size. She had lost about 20 pounds in weight. Only 2 scanty menstrual periods followed the birth of her last child 2 years previouslv.

Physical examination showed a hard, slightly tender, freely movable mass measuring 3 by 5 centimeters located in the upper inner quadrant of the

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 3. The recurrent carcinoma was widely excised. The tumor had invaded the underlying ribs, and parts of the sternum together with the third, fourth, fifth, sixth, and seventh ribs were resected, and the pericardium and left pleural cavity exposed.

Fig. 4. The pericardium was tacked to the intercostal muscles and fascia covering the sternum, by using interrupted sutures of white silk, so as to form a surface on which a graft could be placed. Although the heart was lifted forward by this tenting procedure, there was no visible interference with its function.

Fig. 5. The large operative defect of the chest wall was somewhat reduced in size by approximating the corners. Two heavy split thickness skin grafts cut from the thigh were used to cover the defect which measured 8 inches in width and 9 inches in length.

left breast. Although several axillary lymph nodes were palpable, they were not interpreted as metastases. She had hypertensive cardiovascular disease. The blood pressure was 290 systolic and 140 diastolic. A roentgenogram showed the heart to be moderately enlarged. The aorta was tortuous. There was a harsh blowing systolic murmur heard over the entire precordium. Serologic tests for syphilis were strongly positive.

A radical mastectomy was performed by use of a "wide en bloc excision." Since the skin flaps could be approximated, a skin graft was not used. Pathologic sections disclosed an "adenocarcinoma of the breast without axillary metastases." During the convalescence, she received 2000 roentgen units of irradiation through two ports.

She remained well for almost 1 year. Upon returning for a checkup examination on January 4, 1946, she was found to have a hard, fixed, neoplastic mass in the skin and sternum overlying the junctions of the second and third ribs on the left side (Figs. 6a, b). A roentgenogram of the chest showed the "heart to be tremendously enlarged in its transverse diameter." No destruction of the sternum or ribs was discernible.

Operation. On January 6, 1946, with the patient anesthetized with ether, a closed system being used, an incision was made to encircle widely the recurrent carcinoma. The medial parts of the second and third ribs, together with the left lateral margin of the sternum and manubrium were resected. The pleura was opened. The great vessels at the base of the heart appeared normal. No pleural implants could be felt.

The remaining breast was thin and pendulous (Fig. 6a) and could be readily mobilized upward. A direct transfer single pedicle flap was measured and outlined with brilliant green (Fig. 7). It was then incised, transposed and sutured to cover the operative defect, two rows of interrupted sutures of silk being used. The area from which the flap was taken was closed in a similar manner by drawing the breast upward (Fig. 8). Pathologic sections disclosed a recurrent adenocarcinoma of the sternum and ribs. All incisions healed *per primam* and the patient was discharged on the tenth postoperative day (Fig. 6c).

PRIMARY TUMORS ARISING IN THE CHEST WALL

Many of the common *benign tumors* have been found to arise in the chest wall. The most important, however, are those which arise from the bones. Simple osteomas have been described, but in many instances cartilage is present and, therefore, these tumors should be classified as enchondromas. Some are malignant, and this is particularly true of the cartilaginous tumors which arise in the costal cartilages or the scapula. They may become tremendous in size even when they are benign and may produce pressure against

a b c

Fig. 6. Case 2. a, b, Recurrent carcinoma of the skin, sternum, manubrium, and ribs following radical mastectomy performed 1 year previously. c, Recurrence was excised and defect covered immediately with a direct transfer single pedicle flap from the opposite chest wall. Photograph taken on ninth postoperative day.

other structures; on other occasions, marked deformities develop. Extirpation of these tumors should never be undertaken lightly, for one may have to remove a large portion of the chest wall (Fig. 9). The most common malignant tumor arising in the chest wall is a *sarcoma*, practically all varieties of which have been observed in this location by Hedblom. In a series of 213 cases of tumors of the bony chest wall, Hedblom found 131 to be sarcoma.

Carcinomas of the chest wall, exclusive of those which arise in the mammary gland, in the skin, or in the axilla, are never primary (4).

OBLITERATION OF EMPYEMA CAVITIES; CLOSURE OF BRONCHIAL FISTULAS.

Empyema. The primary object in the treatment of acute empyema is first to save the life

Fig. 7. The recurrent carcinoma was removed by resecting parts of the manubrium, sternum, second and third ribs. The great vessels at the base of the heart were exposed. A flap from the right chest wall was outlined with brilliant green.

Fig. 8. A direct transfer single pedicle flap from the right upper chest wall was transposed and sutured in position to cover the operative defect, two rows of interrupted silk sutures being used. By drawing the right breast upward, the donor area could be closed.

a b c

Fig. 9. A 36 year old white man with a sarcoma of the posterior chest wall which had grown from a walnut-sized mass to its present dimensions in 2 years, a, b. Repeated hemorrhages from the tumor hastened his admission to the hospital. X-ray films showed no destruction of the spine or ribs. The tumor was widely excised and the defect covered with two heavy split skin grafts, c. Photograph on sixth postoperative day; sutures not yet removed.

of the patient, and second, to prevent chronicity. A frequent cause of chronic empyema is failure to provide adequate drainage. Other contributing factors are the presence of foreign bodies or cavities, which cannot be obliterated because of fibrosis of the lung and fixation of the mediastinum or the rigidity of the overlying chest wall preventing approximation with the lung, or conversely by the rigidity of the lung. Many of the operations designed for the correction and treatment of chronic empyema are based on the principle of freeing the rigid walls of the cavity to permit approximation of the tissues and healing by the formation of scar tissue. The Estlander operation involves removal of the overlying ribs, a procedure not always adequate since the underlying parietal pleura may be so greatly thickened that collapse of the chest wall will not occur unless the pleura is also removed. The Schede operation is designed for removal of the thickened parietal pleura. The principle of the Delorme operation is the removal of the rigid surface of the visceral pleura from the lung in order to permit it to expand enough to contribute to obliteration of the cavity.

Bronchial fistulas frequently follow operations for empyema or lung abscess as residual communications between the bronchus and the skin. While serious hemorrhages may occur from the mouth of the fistula, the chief complaint of the patient is the inconvenience caused by wearing a dressing. Of greater importance is the serious danger of immersion of the fistula in water, which may result in drowning by the entrance of water directly into the lungs through the external opening.

There is a tendency for all, especially the smaller, bronchial fistulas to heal as the result of circular contraction of the peribronchial tissue and of the scar tissue around the mouth of the fistula, shown experimentally by Bettman, James, Tannenbaum, and Slobe. Consequently a period of several months should elapse before operative closure is undertaken. However, if a large bronchial opening becomes adherent to the skin, it is less likely to close spontaneously than if it were deeply situated, and in some instances the fistula persists. Graham and Blades have found that repeated cauterizations of the bronchial fistula are usually ineffective. Some fistulas may be closed with several rows of sutures after the lung has been freed from its attachments to the chest wall, a procedure which will permit the contraction of scar tissue to aid in the closure.

In many instances, more extensive reconstructive procedures, occasionally involving partial resection of the lung, are necessary for the permanent closure of the fistulas. When the decision has been made to close a fistula surgically, the operation should be preceded by attempts to determine the size, extent, and contour of the fistula, and the presence or absence of a foreign body. Since the transposition of a skin, or skin and muscle, flap is a simple procedure, it would seem that this is the method of choice, especially when the bron-

Fig. 10. Case 3. a, b, e, Deformity of the chest wall resulting from two operative procedures to drain an empyema and lung abscess, and from four subsequent operations performed to close the persistent bronchial fistula. A communication with a bronchus can best be seen in b. A pectoral muscle flap was transposed to fill the defect. Condition prior to discharge, c, d, taken on the eleventh postoperative day.

chial fistula leads into a pulmonary cavity of considerable size. The success encountered by this means in the elimination of long standing bronchial fistulas resistant to lesser procedures is illustrated in the following case.

CASE 3. A 24 year old white man was admitted to the hospital January 15, 1945. He had had "pneumonia" in 1936, 1937, 1938, and, when first seen here on February 25, 1941, he had the signs, symptoms, and findings of a large empyema on the right side. The anterior portions of the fifth and sixth ribs were resected to establish open drainage, and, subsequently, parts of the fourth and seventh ribs were removed to drain a large lung abscess. During the following months, the patient developed multiple bronchial fistulas which persisted even though 4 ad

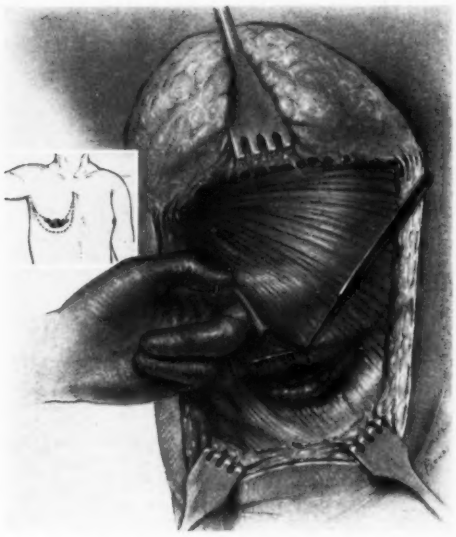


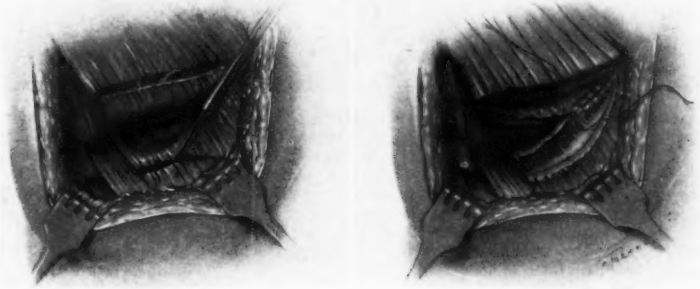
Fig. 11. Insert shows the horseshoe shaped incisions used to excise the scars resulting from the previous operations. A large skin and subcutaneous tissue flap was mobilized superiorly to the clavicle. The pectoralis major was incised beginning about 3 centimeters above the superior border of the pulmonary cavity and continued upward, as shown by dotted line, along the right lateral border of the sternum, and the clavicular attachment was freed superiorly.

Fig. 13. The pectoral muscle flap was transposed laterally and inferiorly in order to obtain the necessary length to cover completely and reinforce the first line of sutures. The flap was then anchored in its new position to the originally incised inferior muscle margin. The heavy skin and subcutaneous tissue flap was then sutured to the inferior incised margin with interrupted sutures of silk.

ditional operations were performed in 3 years in an attempt to close them. Hemorrhage from the mouth of the cavity hastened the present admission.

The right chest wall was markedly deformed due to previous operations, the chronic empyema, and the bronchial fistulas (Fig. 10a, b, e). He had to wear a dressing constantly. He could not take a tub bath or go swimming for fear of drowning, and when smoking, it was embarrassing to him and disconcerting to others to see the smoke curl from beneath his clothing.

On January 19, 1945, the following operation was carried out under pentothal-nitrous oxide-ether anesthesia. The scars resulting from the previous operations were removed by using horseshoe shaped elliptical incisions, as shown in the insert (Fig. 11).



a b

Fig. 12. The muscle was incised about 3 centimeters above and below the margins of the pulmonary cavity, a. The muscle flaps were mobilized toward each other and sutured with interrupted silk, b.

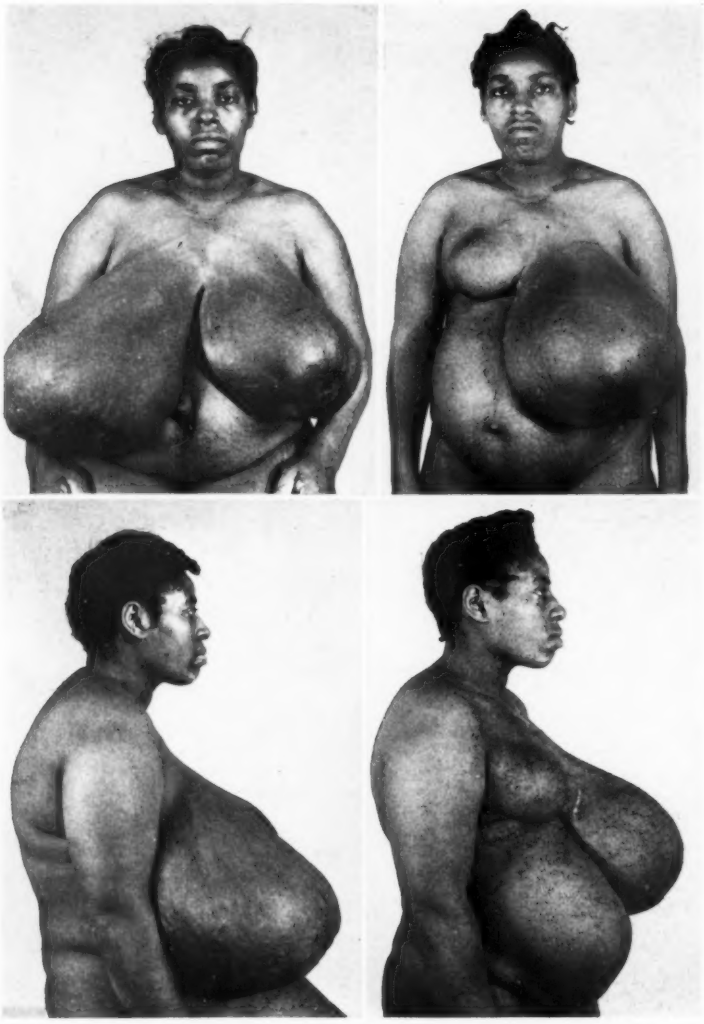


Fig. 14. Gravid hypertrophy of the breasts occurring in a 22 year old colored woman. Although there was some increase in size associated with the progression of pregnancy, it was not until she had reached the seventh month that her breasts began to increase rapidly in size, and within 3 to 4 weeks had assumed tremendous proportions. The breasts did not regress during the postpartum period. The patient was almost completely incapacitated; any movement was laborious and awkward. A right mammoplasty was performed. The specimen weighed 32 pounds (14.5 kilos.). Since it was not advisable to transpose the nipple nor to use it as a free graft, an artificial nipple and areola were constructed.

A large, heavy pectoral skin and subcutaneous tissue flap was elevated superiorly and the inferior border was undermined and mobilized (Fig. 11). The pectoralis major was incised about 3 centimeters above and 3 centimeters below the borders of the pulmonary cavity (Fig. 12a). These flaps were mobilized and then turned inward and sutured with interrupted sutures of silk partially to obliterate the

cavity (Fig. 12b). A pectoral muscle flap was then elevated by incising the muscle along the lateral margin of the sternum medially, and the clavicular attachment was freed superiorly (Fig. 11). The entire muscle flap was mobilized and rotated laterally and inferiorly to obtain the necessary length to cover completely and reinforce the first line of sutures. The flap was then anchored in its new position to the originally incised inferior muscle margin (Fig. 13). Interrupted sutures of silk were used. The heavy skin flap was treated in a similar manner. No drains were inserted. Primary healing occurred and the patient was discharged 12 days after the operation. He has remained entirely well.

RECONSTRUCTIVE SURGERY OF HYPERTROPHIED PENDULOUS BREASTS

Benign and malignant breast tumors have at least one feature in common: they are formed by abnormal and purposeless multiplication of cells previously derived from normal cells. Benign tumors resemble closely the tissue from which they originate. The cells are arranged in a relatively orderly fashion, and although the tumor may attain great size, it rarely jeopardizes the life of the host except by interference with vital functions by pressure. In contrast, malignant neoplasms consist of abnormal cells which may tend to approach the undifferentiated embryonic type. They are not orderly in growth, but invade and destroy adjacent tissues or metastasize to distant parts of the body, and finally lead to the death of the patient.

Massive hypertrophied breasts are, in most instances, comparable to benign tumors and should be considered and treated as such. The increased size may be due to enormous deposits of fat, or, to marked proliferation, hyperplasia, and hypertrophy of the breast tissue proper (Fig. 14). Massive breasts not only incapacitate the bearer but are conspicuous and unsightly. The breasts cause self-consciousness in the bearer, are a source of pain and discomfort, and may cause scoliosis, kyphosis, or lordosis. The excessive perspiration is unpleasant, and the patients avoid society, become depressed and morose, and an ensuing psychosis may develop.

Surgical removal or correction of hypertrophied breasts is just as real and as fully justifiable, especially in young women, as the indication for many ordinary or well recognized surgical procedures, such as the correction of gynecomastia in the male, or the reduction in size of an elephantoid extremity due to lymphatic obstruction. Rather than simply to amputate such breasts, it is much better to remove them in a manner that leaves a pleasing instead of an ugly appearance at their site, if this can be accomplished without increase in the risk. Reconstruction of enlarged breasts is indicated when the hypertrophy leads to a disfiguring or disabling deformity and when there is a reasonable probability that the operation will restore the affected parts approximately to normal without undue danger to the patient. The operation is designed to restore physical as well as psychological balance, and properly executed, it will accomplish these objectives.

In the technique for the correction of massive breasts by partial removal, there are many variations in procedures and many details helpful in obtaining the desired final result. Some of these have been described by Thorek, Maliniac, Lamont, Pickrell, and others. In some instances, satisfactory results in the treatment of massive hypertrophy of the breasts can be attained only by subtotal excision of the enlarged organs and construction of an artificial nipple (Fig. 14).

Virginal and gravid hypertrophy. While the majority of cases of virginal hypertrophy have their onset during adolescence, a similar condition may also occur during pregnancy. Virginal hypertrophy must be distinguished from adipose breasts. Enlargement of the breasts due to deposition of fat may occur in cases of pituitary disturbance, where there is an increase of fat about the hips and in the mammary glands, but the excessive growth seen in virginal hypertrophy does not occur.

"Because the end-organ rather than the hormonial functions is at fault in virginal and gravid hypertrophy, endocrine therapy is unsuccessful" (3). Surgery, therefore, is the only alternative.

CONCLUSION

There are many conditions of the chest wall which can be greatly benefited by the application of specialized plastic surgical techniques. While the foregoing presentation is selective, we have briefly described the procedures em-

ployed in the treatment of four specific conditions, namely, (1) recurrent carcinoma of the breast, (2) sarcoma of the chest wall, (3) persistent bronchial fistula, and (4) hypertrophy of the breast.

A case is presented in which a skin graft was used successfully to cover the pericardium following excision of a recurrent carcinoma of the chest wall.

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PROTECTIVE ACTION OF SULFANILAMIDE ON EXPERIMENTAL CHLOROFORM HEPATITIS

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DIFFERENT substances exist which exert or display a protective action against experimental chloroform intoxication. Methionine and cystine decrease the degree of hepatic injury and the mortality rate produced by chloroform in hypoproteinemic dogs (10). Xanthine and sodium ricinoleate increase the resistance of rats against the toxic action of carbon tetrachloride and chloroform (7). The same investigators found that sulfanilamide given orally to rats protects them against the chronic carbon tetrachloride intoxication as measured by the degree of liver cirrhosis and the mortality rate. The protective action is shown by the mild liver necrosis always observed in the sulfanilamide fed rats as compared with the controls. The protection seems to be due to the sulfonamide group. P-amino benzoic acid does not interfere with the protective action exerted by sulfanilamide.

Forbes and Evans (5) studied the action of sulfanilamide against the liver injury produced by chloroform inhalation in rats. They classified results according to the degree of liver central necrosis revealed on the histologic examination.

After an extensive study, we found that chloroform anesthesia of 1 hour's duration in dogs produces a hepatic lesion (hyaline central necrosis) which is followed, after 3 weeks, by a

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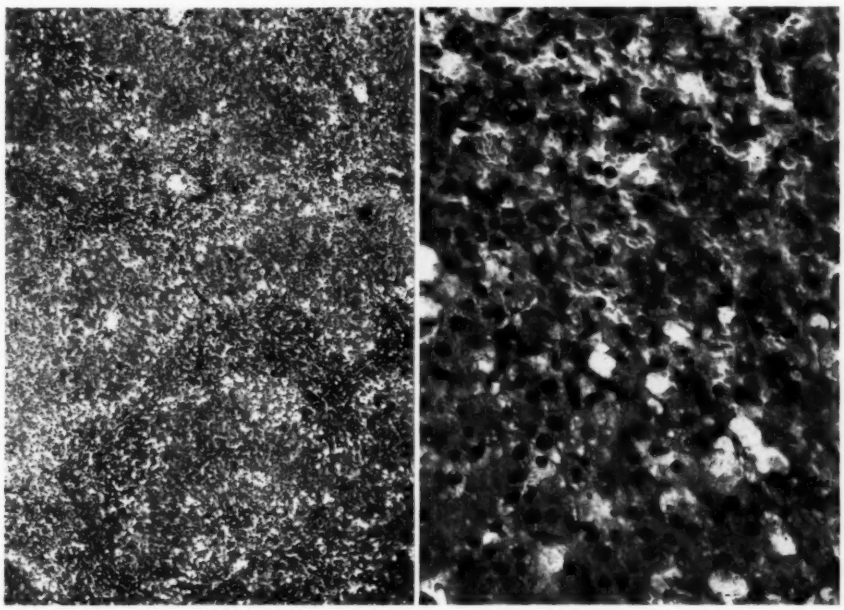

Fig. 1. Dog 511 (control). a, left, Biopsy of liver. Low power view 48 hours after anesthesia. Central hyaline necrosis. b, High power showing nuclear disintegration cytolysis and some mitotic figures.

TABLE I

		Dog No. 517 8.4 kgm.		Dog No. 527 8 kgm.		Dog No. 530 8 kgm.		Dog No. 512 8.6 kgm.		Dog No. 476 8.4 kgm.		Dog No. 520 6.2 kgm.		Dog No. 636 8 kgm.		Dog No. 652 6.6 kgm.		Dog No. 611 6.8 kgm. (+)	
	Days	Prot. %	Sulfa mgm. %	Prot. %	Sulfa mgm. %	Prot. %	Sulfa mgm. %	Prot. %	Sulfa mgm. %	Prot. %	Sulfa mgm. %	Prot. %	Sulfa mgm. %	Prot. %	Sulfa mgm. %	Prot. %	Sulfa mgm. %	Prot %	Sulfa mgm. %
Dogs treated with sulfanilamide	1	94.1	—	123	—	—	—	—	—	—	—	98	—	—	—	—	—	—	—
	2	—	—	102	—	92	—	85.6	—	98	—	—	—	—	—	—	—	—	—
	3(x)	—	—	—	12.45	—	—	—	—	—	—	—	—	95.6	—	81.8	—	—	—
	4	—	9.41	—	—	—	16.50	—	17.50	—	10.05	—	7.67	—	—	—	—	82	—
	5	—	—	—	—	—	—	—	20.20	—	—	—	—	—	—	—	—	—	—
	6(xx)	100	18.83	98.6	19.52	81.3	14.13	75	5.04	110	13.05	107	8.59	89	11.86	93	32.96	—	2.14
	7	40.1	1.94	6.6	3.36	26	2.27	31	—	83.1	2.55	51.8	2.30	28.7	2.96	35.5	8.07	3.5	3.62
	8	67(.)	0.56	25.5	—	51	0.84	20	—	97	0.07	42.7	—	26.6	0.65	30.7	1.56	3.5	0.74
	9		—	53	—	72.6	—	41.3	—	116	—	65	—	30.8	—	53.6	0.57	17	—
	10		—	107	—	—	—	—	—	—	—	80	—	—	—	—	—	64	—
	11		—	—	—	—	—	—	—	—	—	127	—	—	—	—	—	86	—

	Days	Dog No. 511 9.4 kgm. Prot. %	Dog No. 532 8 kgm. Prot. %	Dog No. 525 8 kgm. Prot. %	Dog No. 506 12 kgm. Prot. %	Dog No. 490 8 kgm. Prot. %	Dog No. 516 6.4 kgm. Prot. %	Dog No. 641 8.6 kgm. Prot. %	Dog No. 655 7 kgm. Prot. %	Dog No. 614 9 kgm. Prot. %
Control dogs (not treated with sulfanilamide)	1	107	—	—	—	—	92.3	—	—	—
	2	—	102	78	112.5	95	—	—	—	—
	3(x)	—	—	—	—	—	—	77.3	85	—
	4	—	—	—	—	—	—	—	—	83
	5	—	—	—	—	—	—	—	—	—
	6(xx)	98.8	84	82 (..)	75	108	83.8	71	75	—
	7	3.6	0.2 (..)		13.6	3.5	2.2	no clot (..)	2	2.2
	8	9.4 (.)			10	4.3(..)	2.9		3.2 (..)	3.2
	9				23		13.5			12
	10				—		28.7			28
	11				—		71.3			69
"Protective Index"		+45.5	+6.4		+19	+79.5	+39.8	+26	+28.7	+1.3

(x) Beginning of the fasting period.
(xx) Anesthesia
(.) Dogs Nos. 517 and 511 sacrificed for histological study.

(..) Dog No. 532.—Died 30 hours after anesthesia
Dog No. 525.—Died during anesthesia
Dog No. 490.—Vomits after anesthesia. Died 48 hours after anesthesia.
Dog No. 641.—Died 30 hours after anesthesia
Dog No. 655.—Died 24 hours after anesthesia
(+) Dog No. 611.—Sulfanilamide given 1 hour prior to anesthesia

complete histological recovery of the parenchyma, although regeneration by rapid multiplication of the remaining hepatic cells replaces the greater part of the functional deficit of the organ within 6 days (3, 4). In these instances hypoprothrombinemia is an early index of the hepatic damage produced by chloroform. The lowest values are obtained 24 to 48 hours following anesthesia. By the fifth day (or at most, the sixth) the prothrombinemia has reverted to its normal value. Its variations closely indicate the course of injury as well as the reactive capacity of the liver (12).

In the present work we have studied the protective action of sulfanilamide on liver injury produced by chloroform anesthesia in dogs as well as the degree of hepatic insufficiency and protection by sulfanilamide as measured by the variations in prothrombinemia as compared with controls.

METHODS

Two groups of normal dogs which had been fasted for 3 days (water at will) were used. One group received orally 150 milligrams of sulfanilamide per kilogram of body weight daily during 5 days prior to the anesthesia. The other group served as a control. Each pair of dogs (sulfanilamide and control) was subjected at the same time to chloroform anesthesia of 1 hour's duration. A Boyle apparatus was used in order to minimize the variations imputable to the anesthesia itself. The blood concentration of sulfanilamide was determined periodically during the period of treatment and after the anesthesia by using the method of Banfi and Loncharich (2). The variations of prothrombinemia were followed in the same samples of blood drawn during the experimental period. The method of Tanturi and Banfi was used for the last purpose (11).

RESULTS

In Table I are shown the results obtained in 8 control dogs subjected to a chloroform anesthesia; 5 died within 24 to 48 hours after the anesthesia. All dogs previously fed with sulfanilamide survived. The decrease in prothrom-

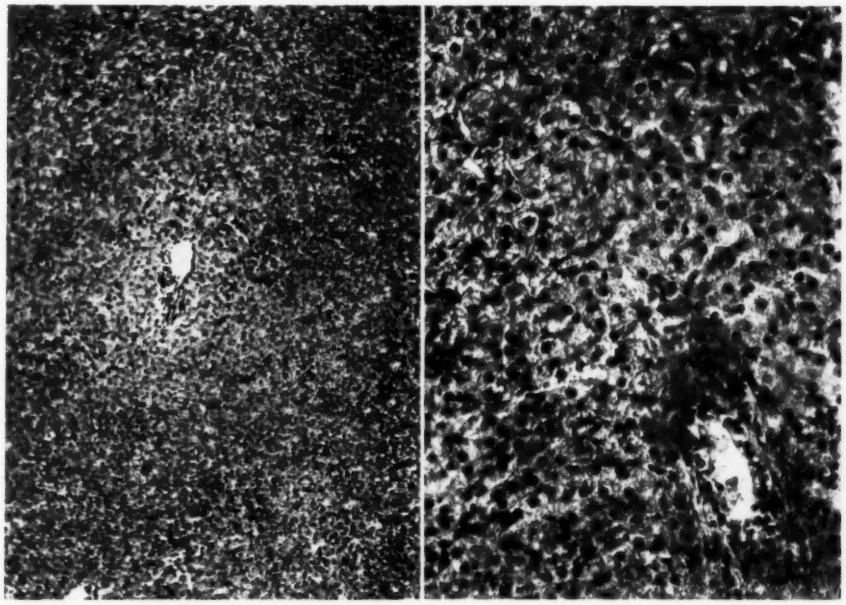

Fig. 2. Dog 517 (sulfanilamide). a, left, Biopsy of liver. Low power view 48 hours after anesthesia. Very mild injury. b, High power showing no nuclear derangement and almost normal architecture.

binemia produced by chloroform was less in the sulfanilamide group than in the controls.

The degree of "protection" is expressed by the difference between the lowest concentrations of prothrombin reached after the anesthesia in the sulfanilamide fed dog and in the control. The "protective index" thus obtained gives a fairly approximate figure of the protection conferred. In every instance the favorable influence exerted by sulfanilamide is shown. The "protective index" varies from +6.4 to +79.5, averaging +35. This average was calculated by excluding the results obtained in the pair of dogs 611 and 614 because in this instance sulfanilamide was administered 1 hour prior to the anesthesia. If sulfanilamide is given 1 hour prior or during the anesthesia, the drug does not exert any protective action.

The effect exerted by sulfanilamide is shown during the first 24 hour period after the anesthesia. During this period the control dogs regularly vomit and are depressed. These symptoms were not observed in the sulfanilamide group. The photomicrographs show pieces of liver tissue obtained 48 hours after the anesthesia. The degree of hepatic necrosis was less in the sulfanilamide treated group if compared with the control.

COMMENT

The results obtained clearly show that sulfanilamide exerts a protective action against liver injury produced by chloroform in dogs. The degree of liver injury, its course, the reactive capacity, and the protection conferred can be accurately measured following the variations in prothrombinemia. When sulfanilamide is administered at the same time or 1 hour prior to the anesthesia, the protective action is not observed which suggests that the action displayed by the sulfanilamide is not a direct one through the liver parenchyma. McIver (9) has shown that thyroxin increases the susceptibility of rats to chloroform intoxication. Earlier works on chloroform liver injury in dogs also pointed out the increased susceptibility to chloroform of the animals previously fed with thyroxin. Several investigators (1, 8) showed that sulfanilamide de-

presses the basal metabolic rate in rats by producing an increase in size of the thyroid gland and decrease of "colloid." From these studies Forbes presumes that the action of sulfanilamide in protecting the liver against the chloroform injury is due to the decreased susceptibility obtained through a thyroid depressing effect of sulfanilamide. If the same hypothesis is to be used to explain the results obtained in dogs, it must be submitted to experimental investigation.

Many clinical cases of liver necrosis due to sulfanilamide were reported in the literature. However, some authors recommend the use of the drug in biliary infection. To the present time no experimental animal is suitable for producing a liver injury with sulfa drugs. We were not able to produce a liver injury with any dose of sulfanilamide in dogs. This leads us to presume that human susceptibility to sulfa drugs stands by itself. Therefore, the mechanism by which the protective action of sulfanilamide is exerted against chloroform liver injury in dogs would explain many of the contradictory findings found in the literature concerning the toxic action of sulfanilamide on human liver. Further investigations are required.

CONCLUSIONS

1. Sulfanilamide given daily to dogs prior to a chloroform anesthesia of 1 hour's duration decreases the degree of liver injury regularly produced by chloroform. In this experimental condition hypoprothrombinemia and histological changes are less severe than in the control animals.

2. The degree of protection obtained with sulfanilamide can be accurately expressed by the "protective index" which results from the difference between the lowest figures of prothrombinemia obtained in the sulfanilamide-fed dog and the control.

3. Sulfanilamide given to dogs during the time of the anesthesia does not protect against liver injury produced by chloroform.

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GASTRIC CARCINOMA

A Comparative Review of the Origin, Diagnosis, and End-Results in 583 Patients

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AFTER the third decade, neoplasm is second only to cardiovascular disease as a cause of death. Since about one-fifth of this mortality is due to carcinoma of the stomach, the subject is of prime importance and worthy of constant, repeated analytical study.

In a review covering 444 patients with carcinoma of the stomach discharged from the Fourth Medical and Surgical Division of Bellevue between 1919 and 1938, the dismal outlook was pointed out (2). The purpose of this review is to investigate whether the past 7 years has altered the status of the patient with gastric carcinoma. From 1939 through 1945, of 171 patients discharged with the diagnosis of carcinoma of the stomach, 32 were eliminated because of insufficient diagnostic proof.

The diagnosis in the remaining 139 cases was verified by pathological specimen and unquestionable x-ray evidence. Of these (Fig. 1) 76 (64.3%) were considered inoperable, following admission. The reasons for inoperability were: 14 were moribund; 22 had extreme cachexia or senility; 28 showed extensive lesions with metastases; and 12 refused operation. Forty-three per cent of these patients died while on the wards[1].

The remaining 51 cases (36.7%) were considered operable. An effort was made to do an exploratory operation in every case in which any hope for improvement by surgical intervention was thought possible. Exploratory laparotomy in 22 cases (15.5%) proved that no further operative measure could be undertaken. On 10 patients a palliative procedure was performed, as temporary relief for obstructive lesions.

[1]For purposes of this study, it is considered a mortality if the patient does not leave the hospital, regardless of the cause of death or length of time following operation.

In only 19 patients was gastric resection feasible. Whenever possible, wide resection was performed, even though evidence of malignant extenson, such as enlarged nodes (which were probably neoplastic) were present. This group had a mortality of 62.3 per cent. Resection was possible in 13.7 per cent of the total number of cases, and in approximately 38 per cent of the operable cases. Only 7 patients (5%) were discharged from the hospital as possible cures.

The symptoms in our present series are approximately the same as those found in our previous series of patients. Pain, loss of weight, vomiting, and weakness remain the predominant reasons for seeking medical care and hospitalization. In an effort to evaluate further, we have attempted to divide the relative time of the onset of the various signs and symptoms (Table I) into "early" and "late." Pain and loss of weight head the list of early complaints, while cachexia and a palpable mass are the common late findings. The value of this compilation is questionable. Many of the signs and symptoms which are early for one patient are late for another. It is clear that it will be necessary to find and utilize means and methods other than these signs and symptoms if we are ever to diagnose gastric carcinoma early.

This conclusion is further borne out by a study of the relationship between the duration of the signs and symptoms, the operability, and the resectability of our patients (Table II).

As was also shown in our previous studies, a graphic representation (Fig. 2) of the percentage relationship between operability, resectability, and the lapse of time after the patient's first complaint does not influence the possibility of cure. Resectability cannot be prognosticated by what we now consider

TABLE I.—SIGNS AND SYMPTOMS*

Sign and symptom	Early	Late	Total	Percentage
Pain (epigastric discomfort)	123	11	134	96
Loss of weight	90	27	117	84
Vomiting	51	36	87	62
Palpable mass	9	58	67	48
Weakness	34	29	63	45
Anorexia	51	11	62	45
Cachexia	4	34	38	27
Nausea (only)	23	5	28	20
Eructation	22	2	24	17
Hematemesis	6	12	18	13
Melena	4	13	17	12

*Signs and symptoms due to metastases or extension of malignancy, i.e. jaundice, ascites, etc. have not been listed.

symptomatology. In the overwhelming majority of cases, our present criteria allow us to make a diagnosis only in the late cases, and as we continue to depend on inadequate methods, it is only by purest accident that early cases come to operation. Since waiting for clinical signs and symptoms to appear has resulted in low rates of operability and resectability regardless of their duration, further attempts to increase our diagnostic accuracy dependent on complaints of the patient are doomed to failure.

GASTRIC ANALYSIS

Gastric analysis was performed in 63 cases. Fifty-five (87%) showed marked hypoacidity or achlorhydria, 6 (8%) showed normal acidity, and 2 (3%) showed hyperacidity. In view of the frequency of hypoacidity in normal people over 50 years of age, the findings in this test are not diagnostic; however, a decrease or an absence of free hydrochloric acid must arouse strong suspicion, and necessitates the positive exclusion of carcinoma. The possibility of cancer occurring in the presence of normal and increased acidity has been called to our attention. The high percentage of cases of hypoacidity or achlorhydria in both of our studies is perhaps indicative of the number of patients with advanced type of cancer admitted to Bellevue Hospital. In consideration of the simplicity of this procedure, gastric analysis should be part of a routine examination of all those in the cancer age group.

X-RAY EXAMINATION

X-ray examination of the stomach with contrast media was carried out in 124 of the 139 cases. One hundred twelve showed roentgenologic evidence of gastric malignancy, a diagnostic accuracy of more than 90 per cent. Of the 12 cases eventually diagnosed as carcinoma by autopsy or laparotomy: 7 were reported as negative, 3 were diagnosed as ulcer of the stomach, 1 as an extragastric tumor, and 1 as a benign tumor of the stomach.

During the 7 years covering our present study there has been a large increase (approximately 30%) in the number of patients subjected to x-ray examination for gastric disease. An increasing percentage of cases are correctly diagnosed by fluoroscopic and x-ray examination. The roentgenologist has proved himself vastly superior to the clinician in diagnosis, and the asymptomatic patient will only come to operation subsequent to discovery of the condition by x-ray examination (9).

A comparison of the percentage (Fig. 3) of operable cases and the possibility of cure during the past 7 years (Series A) with the previous 20 years (Series B) shows a decided similarity. With the exception of the increase in resectability (2.2% to 5%), there is no statistically important change. The rate of operability remains approximately the same (33.4% to 36.7%).

Without any attempt to excuse our poor results, it must be considered that the cases studied were of consecutive admissions, and many had been diagnosed elsewhere. Thirty-nine (28%) were considered unresectable by previous laparotomy or clinical examination, prior to admission to the hospital. If this number is subtracted from our total, it raises the percentage of operability from 36.7 to approximately 50 per cent and the percentage of resectability from 13.7 to 19 per cent. Even this increase in the percentage of operable and resectable cases, as compared with the results of our previous series (Series B) should not lead to the conclusion that the status of these patients has changed. The supposed improvement is more apparent than real. It cannot be considered as due to earlier diagnosis or therapeutic advance, in view of the end-results. In our opinion any increase in oper-

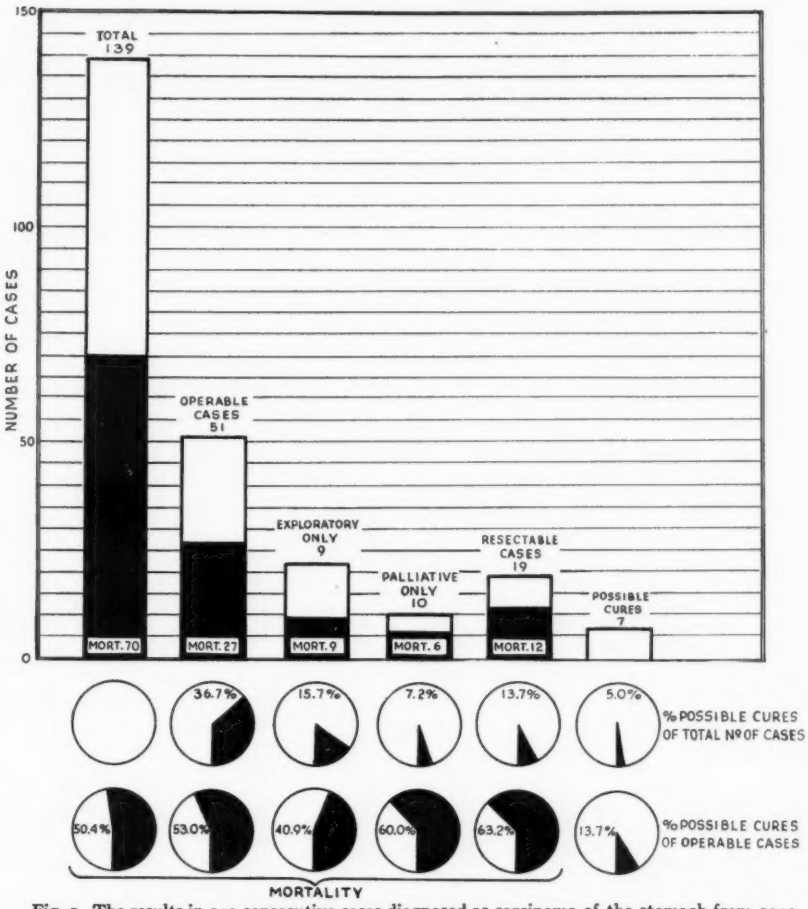

Fig. 1. The results in 139 consecutive cases diagnosed as carcinoma of the stomach from 1939 to 1945, Series B.

ability and decrease in mortality is due to improved techniques utilized in preoperative and postoperative care (i.e., intravenous plasma, proteins, amino acids, vitamins, frequent transfusions, Wangensteen drainage, etc.). The institution of an anesthesia service at Bellevue Hospital, with trained anesthetists who visit the patients both preoperatively and postoperatively (frequently using positive pressure, paravertebral block, cyclopropane, and curare), has decreased the number of post-anesthetic and postoperative complications.

Although an increased number of patients recover from the operative procedure, this increase is not reflected in the percentage of actual cures. This fact is emphasized by a study in the Fourth Division at Bellevue Hospital of 52 patients with a previous diagnosis of carcinoma of the stomach, who were readmitted subsequently and observed during this same period (1939 to 1945).

Of these 52 patients, 42 were previously operable, exploratory only was performed on 15, palliative procedures on 2 and gastric resections were done on 25. All of these patients either died during their readmission to Bellevue Hospital, or they were transferred, bedridden, to a home for incurables where they

TABLE II.—DURATION OF SYMPTOMS

Length of time	Inoperable	Operable	Resectable
Less than 1 month	9	3	
1 to 3 months	13	9	4
3 to 6 months	15	12	2
6 to 12 months	18	16	5
1 to 2 years	5	2	2
2 to 3 years	5	5	4
3 to 5 years	2	2	
5 to 10 years	2	1	1
Over 10 years	2	1	1
Total	76	51	19

succumbed. None of the patients on whom resection was not done lived longer than 10 months, and the average length of life was 6¼ months. The subsequent course of the 25 patients resected (Table IV) and later readmitted indicates that even though an increase in the percentage of resectability has taken place, the eventual outlook for what we now consider the most favorable cases is bad indeed. A life expectancy of less than 2 years following resection cannot be considered progress in the cure of gastric cancer.

PEPTIC ULCERS

There were 16 cases (11.5% of the total) in which the history made the possibility of malignant degeneration of a benign peptic ulcer a factor for consideration. As in the previous series, in which 17.1 per cent of the patients presented this possibility (as well as in other studies 2, 3, 8, 16, 17, 18), these cases have been carefully investigated. Seven were diagnosed as duodenal ulcers, and as such can either indicate errors in diagnosis or the concomitant existence of a duodenal ulcer and a gastric malignancy near the pylorus. Each of the 9 cases which were diagnosed as gastric ulcer has been reviewed and received exhaustive study. Since the previous report from our gastroenterological clinic (18) concerning the possibility of malignant degeneration of peptic ulcers, we have followed 165 cases of gastric ulcers over periods from 1 to 19 years, and have failed to find a single case in which the transformation from a benign ulcer to a gastric neoplasm could be proved. Extensive investigations have either shown the separate and individual inception of the lesions, or demonstrated the error in the diagnosis of a benign peptic ulcer for what was later proved to have been a malignant lesion from its onset. In several cases of carcinoma of the stomach which we have reviewed, clinical history or x-ray study caused suspicion that they had their origins in peptic ulceration.

TABLE IV.—END-RESULTS IN 25 PATIENTS WITH GASTRIC RESECTION FOR CANCER

Readmitted between 1939 to 1945

Length of time between operative procedure and final readmission.

	No. cases
Less than 3 months	3
Less than 1 year	9
Less than 2 years	10
More than 2 years*	3
Total No. of months	583
Average	23¼ mo.

*One case was readmitted with a period of 288 months between operation for gastric malignancy and death. Without this case the average length of time is reduced to 12¼ months.

TABLE III.—GASTRIC ANALYSIS*

	No. cases
Total	63
Hypoacidity or achylia	55
Normal acidity	6
Hyperacidity	2

*Method: A Levin tube No. 18 was passed through the nose into the stomach, and a fasting specimen of about 30 c.c. collected and labeled as such; ½ c.c. of histamine was injected subcutaneously. A test specimen of about 10 c.c. was then taken and labeled No. 1, and after that at 15 minute intervals additional specimens, to a total of 4 were collected and labeled No. 2, No. 3, and No. 4, respectively.

CASE 1. A 60 year old white male in whom a diagnosis of peptic ulcer had been made 17 years before had had a gastric resection at that time. The patient was admitted to this hospital in February, 1937, because of a recurrence of ulcer symptoms. A gastroscopic examination revealed two ulcerative lesions near the ostia. He was discharged following improvement under medical care. In June, 1938 he returned because of persistent epigastric pain. An exploratory operation was performed, dense adhesions were released, and the stomach was found free of disease by gross examination. Gastroscopic examination in December, 1938 revealed no signs of ulceration, but the development of atrophic gastritis. He was readmitted in 1943, and laparotomy revealed an inoperable malignant lesion of the stomach.

CASE 2. A 47 year old white male, who had had a resection for gastric ulcer in April, 1939, returned because of malfunction of the stoma in March, 1940. A further gastric resection to eliminate the malfunctioning stoma was performed. Three months later he returned to the hospital because of a recurrence of gastric dysfunction; exploration revealed "extensive stony hard lesions on the stomach, liver, peritoneum, and omentum." The pathologist reported carci-

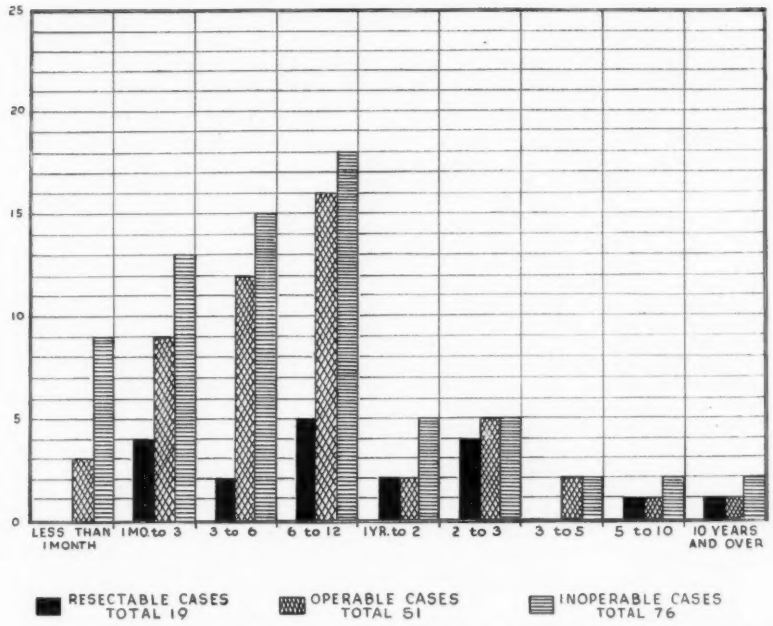

Fig. 2. The relationship of the duration of symptoms to the operability and resectability as indicated by percentages.

noma. At this time, the microscopic sections taken from the stomach at the two previous operative procedures performed in 1937 and 1940 were re-examined by Dr. Douglas Symers, then Director of Pathology in New York City hospitals. He reported that adenocarcinoma was present in all the specimens previously removed and reported as peptic ulcers.

In both of these cases, simple clinical deduction might lead to the belief that malignant degeneration of previously benign lesions had taken place. In one case we have gastroscopic evidence that the ulcerations had healed and atrophic gastritis was present 4 years prior to the patient's admission for a malignant condition. In the second case, a careful pathological review of the microscopic sections from the two previous operations showed that the supposedly benign peptic ulcer had always been malignant.

In 1937 a series of 109 cases of gastric ulcers and 118 cases of gastric cancers were reviewed in search of evidence for the change from benign ulcer to neoplasm (18). Together with this series, since 1919 we have followed 583 patients with carcinoma of the stomach who have been admitted to our wards, and 1,475 cases of peptic ulcer (of which 165 were gastric ulcers) which have been followed in our gastroenterological clinic over a 1 to 19 year period. In none of these cases was it possible to prove that malignancy had its inception in benign ulceration, nor have any of the known ulcers developed malignancy.

Clinical and pathological experience in surgery warns against didactic statements concerning carcinogenesis. Isolated cases in our series might leave reasonable doubt concerning the inception of the malignant condition.

CASE 3. A 43 year old white male with a typical history of peptic ulcer over a 10 year period developed an additional severe pain radiating through the back. X-ray films were interpreted as showing "a large penetrating ulcer of the lesser curvature of the pars media." On resection of the stomach, the lesion was suspected of malignancy on gross examination, and the pathological examination showed adenocarcinoma of the stomach.

From this patient's history, we can conjecture that this man had a peptic ulcer of the stomach over a long period of time, suppos-

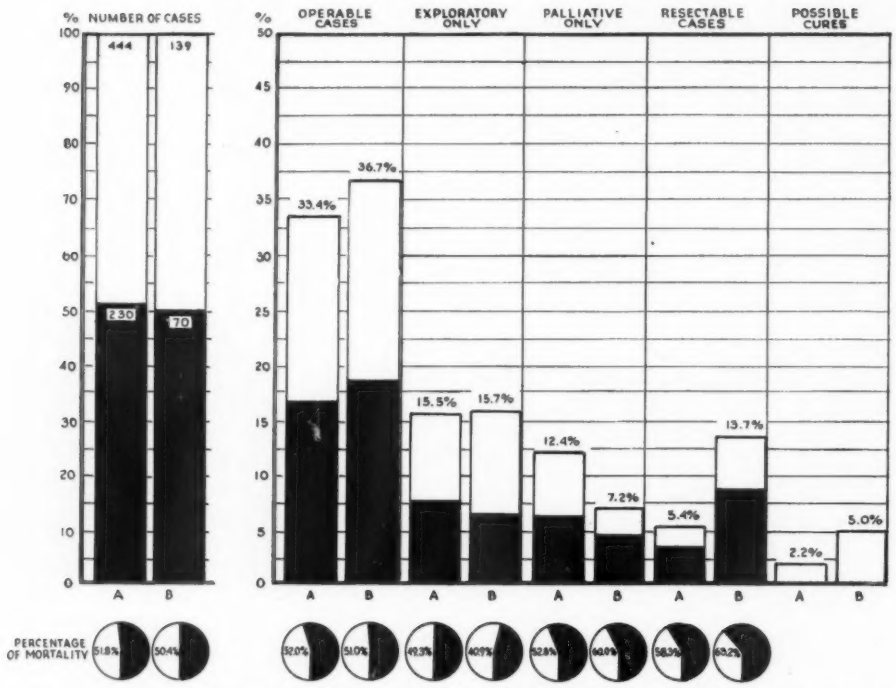

Fig. 3. The comparative results in the treatment of carcinoma of the stomach between 1919 and 1938 (Series A) with those of 1939 and 1945 (Series B).

edly verified by x-ray findings, and later a malignant condition at operation. As to whether this man had both a carcinoma and a peptic ulcer at the same time, or whether he developed a gastritis which underwent neoplastic degeneration, or whether the carcinoma originated at or near the peptic ulcer, we do not know. Several eminent authors (4, 7, 14, 21, 27, 29) on this subject consider that the change from peptic ulcer to malignant lesion occurs frequently. Although it is possible that a neoplasm may arise at the site of the peptic ulcer, in our experience this transformation is not only unusual, but extremely uncommon. Whether a gastric carcinoma is early or late, small or large, it may undergo peptic ulceration, eroding away all signs of malignancy (12), and at this time will give the signs and symptoms of this condition. By x-ray examination it may even be mistaken for benign peptic ulcer, and the malignancy may not be apparent until later. In spite of the fact that we perform gastric resections on many patients, including those with intractable gastric ulceration, as well as in any case in which there is doubt concerning the diagnosis of carcinoma, we do not believe that the potentiality of malignancy originating in a benign peptic ulcer is an indication for operation.

GASTROSCOPY

Gastroscopic examination was attempted in 28 cases. In 22 the diagnosis of carcinoma of the stomach was correctly made. One case was termed "negative," and 1 case diagnosed as gastric ulcer; 4 attempts to perform gastroscopic examination were considered "incomplete" or "unsuccessful" and no report rendered.

The flexible gastroscope allows visualization of the gastric mucosa and is an additional means of verifying the diagnosis of gastric cancer. The interpretation of the results of gastroscopic examination (like the results of

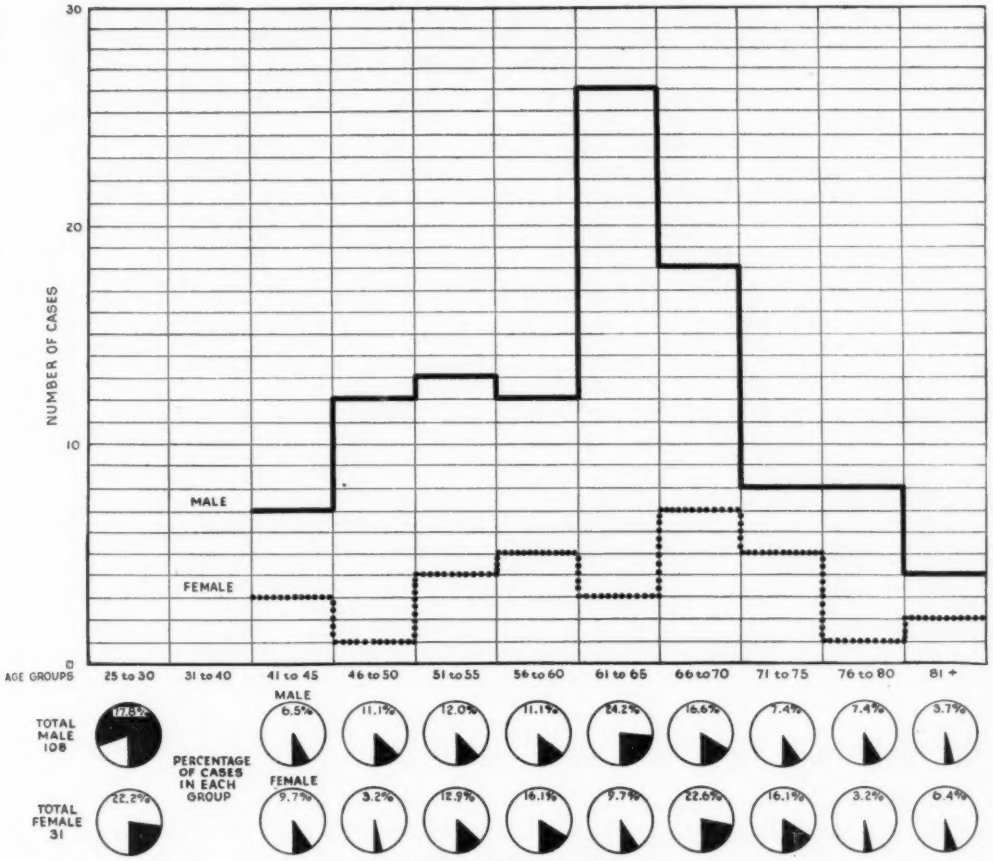

Fig. 4. The age and sex incidence.

any other diagnostic procedure) must be tempered with the knowledge that there is an element of error in the procedure, and also that the accuracy of the observations are dependent on the position of the lesion and the experience of the gastroscopist. However, since any information concerning the condition of the gastric mucosa is of diagnostic importance, gastroscopic examination should be utilized in all lesions of a questionable or controversial nature following x-ray and laboratory studies.

The extensive use of this instrument by experienced observers has verified the findings of Faber and Konjetzny concerning the actuality of involutionary or retrogressive gastritis. Chronic gastritis frequently accompanies gastric ulcers. To clarify a term, gastritis does not necessarily mean an inflammatory lesion, but includes functional and pathological derangements of the glandular elements which make up the involutionary changes. As shown by Judd, definite changes in the mucosa indicative of severe chronic gastritis of long standing are present in association with gastric carcinoma. The origin of gastric cancer on a mucosa which is the seat of this pathological change has been described so frequently (5, 11, 12, 15, 22, 25, 26) during the past 20 years that we believe that this change must be considered an important factor in the vast majority of cases.

Rigler has recently reported on the frequent occurrence (more than 8%) of carcinoma on the atrophic gastric mucosa of patients suffering from pernicious anemia. The age and sex incidence of chronic retrogressive gastritis coincides with the age and sex of the patients in both series of gastric carcinoma which we have reported (1, 3). From our observations it would seem that the instigation of gastric carcinoma is much more closely related to the chronic pathological involutionary changes, which take place in the gastric mucosa, than it is to benign peptic ulceration.

In reports on the endocrine nature of the gastric mucosa (1, 3) we have called attention to massing of cases in the 40 to 70 year old group, and the occurrence of cancer in 3.4 males for each female. Our findings in this review are practically identical with our previous studies (Fig. 4). Although we realize that carcinoma of the stomach occasionally appears in younger people, the great majority of these cases occurs after 40, and the problem of gastric carcinoma lies within this large group.

The preponderance of males and the high incidence in later life in all studies emphasize the endocrine factor in the etiology of gastric neoplasms. During that period in life when gastric carcinoma most frequently occurs there are marked changes of the content and nature of the sex hormones. Experimental work has shown (1, 3) that activity of the gastric mucosa is influenced by hormones, including changes in the androgen-estrogen ratio. Although it is our belief, based on the experimental results and clinical observations of ourselves and others (reviewed in previous publications 1, 3), that the relationship between the hormone control of the gastric mucosa and gastric disease is an important carcinogenic factor, we fully realize that it will take further extensive experimental study to prove the various etiological agents responsible for the change from normal or pathological gastric mucosa to neoplasm.

DISCUSSION

From our findings it is evident that the outlook for the patient with gastric carcinoma continues to be dismal. Any gains that have been made are the result of improved preoperative and postoperative care. Parenteral administration of fluids to control biochemical changes, advances in anesthesia, and the advent of sulfonamides and penicillin have raised the rates of operability and resectability, and lowered the operative mortality, but have not appreciably affected the course of the disease. Comparative studies of the results from more specialized surgical clinics have shown that operability, resectability, and the length of postoperative cure are greatly influenced by the selection of cases (24). But the prognosis of the patients in a large general hospital (which represents a cross-cut of the general population) remain distressingly unfavorable. The lack of time relationship between the onset of symptoms (as we now understand it) and the percentage of resectability reveals that our furthest progress has been our determined effort to diagnose late cases. The problem resolves itself to evolving a means of bringing patients with carcinoma of the stomach to operation early in their pathological course (6, 9, 12), rather than early in their clinical course. At present we operate on a curable carcinoma of the stomach by accident, or because of an extremely fortuitous early diagnosis.

Since our attempts to discover early gastric carcinoma are obviously failures, our efforts should be directed toward the improvement of our methods of diagnosis. At the present time, our only method of revealing asymptomatic curable gastric cancer is by fluoroscopic and x-ray studies. The institution of these studies on a mass scale, by methods similar to those used in mass examinations for tuberculosis, offers a great opportunity to uncover asymptomatic malignant disease. The use of such a procedure has been advocated by several since 1935 (6, 28).

Comparative mass fluoroscopic and x-ray studies on approximately 400 American soldiers and 400 German prisoners with gastrointestinal complaints showed that 1 per cent of the German prisoners had carcinoma of the stomach, while none was found in a similar group of American soldiers (30).[1] Although

[1]It is interesting to note that the average age group of the German prisoners was 34 while among the American soldiers it was 28.

the study of Dailey and Miller on 500 normal people did not reveal any gastric carcinoma, we believe that it must be carried out in groups larger than 1,000 to be statistically valuable, and that routine annual fluoroscopic and x-ray studies of the stomach, especially in the carcinoma age group, should be instituted.

A recent authoritative mass fluoroscopic and x-ray study (28) on a consecutive group of 2,413 patients without gastrointestinal complaints revealed that 3 had asymptomatic gastric cancer. This procedure, conducted on a larger scale, would undoubtedly disclose and bring to operation a higher percentage of resectable and curable patients than any other means at our disposal. The outline of a plan by which mass fluoroscopic and x-ray studies of the stomach could be routinely carried out on an increasing number in the carcinoma age group is proposed.

1. Education of the public (a) on the asymptomatic character of carcinoma of the stomach; (b) on the necessity for routine fluoroscopic and x-ray examination of the stomach.

2. Fluoroscopic and x-ray studies of the stomach performed (a) as part of an annual physical examination in military services; (b) as part of an annual physical examination in veterans' organizations; (c) as part of an annual physical examination in large industries; (d) as part of an annual physical examination on members of labor unions; (e) as part of a physical examination prior to the issuance of health and life insurance policies; (f) as a routine procedure on all patients over 40 years of age entering hospitals.

3. Availability to private physicians of facilities for fluoroscopic and x-ray studies of the stomach for those on every economic level, so that all patients over 40 years of age are given routine annual examinations.

4. Gastric analysis and gastroscopy, as well as further repeated x-ray studies in all questionable or controversial lesions found on fluoroscopic examination.

In our present state of ignorance concerning carcinogenesis in general, and the early diagnosis of gastric carcinoma in particular, the popularization of fluoroscopic and x-ray examinations of the stomach presents an important method of discovering an increasing number of curable cases among the general population.

CONCLUSIONS

1. Comparative studies of 583 cases of carcinoma of the stomach between 1918 and 1945 demonstrate the poor prognosis and emphasize lack of progress.

2. The absence of relationship between the onset of the symptomatology, operability, and possibility of cure reveals our failure in the diagnosis of early cases.

3. Investigation does not substantiate the possibility of the transformation of benign ulcer to gastric carcinoma as anything but a rare occurrence.

4. It is suggested that the following four factors have a definite relationship: (a) age and sex incidence; (b) chronic "gastritis"; (c) endocrine effects on the gastric mucosa; (d) the inception of gastric neoplasm.

5. A plan is presented for the utilization of mass fluoroscopic and x-ray studies of the stomach, as a means of discovering curable malignant conditions.

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THE PHYSIOLOGIC EFFECTS OF CURARE AND ITS USE AS AN ADJUNCT TO ANESTHESIA

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CURARE is still a relatively unknown drug. It is known to cause complete paralysis of the skeletal muscles by inactivating acetylcholine and thus blocking nerve impulses to the voluntary muscles. This paralysis begins with the muscles innervated by the cervical nerves and continues successively through the muscles of the extremities, the abdominal muscles, the intercostals, and finally the diaphragm.

Claude Bernard in 1857 reported that curare is absorbed from subcutaneous, intramuscular, and intravenous injection and by the pulmonary and rectal mucosa, but is not absorbed by the mucosa of the rest of the intestinal tract, the genitourinary tract, or through the skin. Alexander Partos in 1930 reported that curare is detoxified by the liver and can be recovered from the liver substance. He believed the curare not absorbed by the liver was excreted unchanged by the kidneys. This theory agrees with the more recent work of the pharmacologists (Squibb), who have found that 40 to 60 per cent is excreted in the urine.

ANIMAL EXPERIMENTATION

In the last 5 years the use of curare to obtain muscular relaxation in abdominal surgery has become widespread. In order to determine whether curare could safely be used to produce the apnea necessary for "controlled respiration" in intrathoracic operations, in conjunction with nitrous oxide anesthesia, the physiological effects of the drug on dogs were studied. A series of 50 dogs was given enough curare to produce apnea for from 2 to 8 hours. The first 25 dogs were given atropine 0/0006 (gr. 1/100) and the second 25 morphine sulfate 0.015 (gr. ¼), or 0.03 (gr. ½) depending on the size of the dog, and atropine 0/0006 (gr. 1/100). No difference was noted in the amount of curare necessary to produce apnea or the duration of the apnea in the two series.

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An initial intravenous injection of 40 milligrams of curare was given (enough to cause apnea in about 2 minutes). As soon as apnea and muscular relaxation occurred, an endotracheal tube was inserted and connected to a breathing bag and cylinder of oxygen. Artificial respiration was carried on by gentle intermittent pressure on the bag. We consider this a more physiological method than the use of a mechanical respirator. An oxygen flow of 7 to 8 liters per minute was maintained to prevent the accumulation of carbon dioxide in the bag. Further doses of curare were injected intravenously whenever the dogs started to breathe.

The average dose of curare in the first series of 25 dogs was 56 milligrams. Of the series, 6 dogs died, 1 of deliberately produced hypoxia and respiratory acidosis, 1 of an overdose of prostigmine (2 c.c. of 1:2000), 1 of accidental failure to intubate and consequent acute anoxia, and 3 of pulmonary atelectasis after return to the cage. We found that to prevent atelectasis it was necessary to continue artificial respiration until the intercostal muscles were contracting strongly.

The second series of 25 dogs received an average dose of 88 milligrams of curare. Two of these dogs died, 1 of pneumonia during an epidemic in the animal house 4 days after the experiment, and 1 of atelectasis after being returned to the cage. This last animal was deliberately sacrificed in order to impress the students with the importance of continuing artificial respiration until the intercostal muscles recover their power of contraction. In no case could death be attributed to the specific toxicity of curare.

We concluded from this series that curare of itself does not cause death in apneic doses. A

second important discovery was that artificial respiration must be continued until the intercostal muscles are contracting strongly. Discontinuing before this stage of recovery, even though strong diaphragmatic contractions were present and the dogs were able to oxygenate themselves adequately, resulted in death from atelectasis.

Other interesting facts came to our attention during these experiments. Although the dogs were curarized to the point of apnea, if a finger were moved toward the eye, without touching the lashes, hair, or skin, the eyelids would close. A loud noise would often cause a sudden start in a dog apparently completely paralyzed with curare. Therefore, vision and hearing must still be present after curarization and their reflex arcs be intact. It was also noted that the platysma seemed much less affected by curare than the other muscles. Even though the dog was in apnea, a flea crawling on the abdominal wall would cause violent twitching of the platysma in that area. Twitching of the platysma was the first sign of recovery from curare. This was most evident in the animals which had not received morphine. These phenomena raise grave doubts in our minds that apneic doses of curare produce anesthesia or analgesia.

A rise in blood sugar was found after the injection of curare in a series of 6 dogs. The rise averaged 49.9 milligrams per cent. All these animals showed glycosuria but no acetonuria.

Electrocardiograms were taken before, during, and after the repeated administration of curare in a series of 4 dogs. After curare the *QRS* voltage decreased, the *T* waves became variable and, according to the cardiologists, the tracings resembled those seen in potassium poisoning.

Electroencephalograms were taken on a series of 5 dogs and showed identical changes in all. Control tracings were taken 1 hour after premedication with morphine and atropine. A tracing was made while the dog was in apnea following the administration of 40 milligrams of curare. When the dog had recovered from the curare sufficiently to breathe, an anesthetic dose of sodium pentobarbital was injected intravenously and a third set of electroencephalograms was taken. Two days later tracings were repeated, first with morphine and atropine and then with the same dose of pentobarbital as before, without curare. Compared with the control tracings, those taken following curare showed a very marked lowering of the potentials, together with slight dysrhythmia. Light flashed in the eyes or loud noises caused no alteration in the picture unless the dog jumped and moved the leads. After pentobarbital more marked dysrhythmia occurred than with curare. It was concluded that large doses of curare may cause a cerebral dysrhythmia compatible with a slight narcotic effect.

It was found that the repeated administration of curare over long periods of time caused no change in the animal's reaction to the drug. Four dogs received from 6 to 10 administrations of curare each in 6 months' time for periods ranging from 30 minutes to 4 hours. They showed neither increased tolerance nor sensitivity to the drug at the end of this time. After recovery they behaved in all respects like normal animals.

A cesarean section under local anesthesia was performed on a pregnant bitch while she was in apnea induced by 40 milligrams of curare, and 6 pups were delivered. All the pups breathed spontaneously, moved and showed no signs of being curarized. One pup was freed from its membranes and held in the surgeon's hands, the cord pulsating, while another 20 milligrams of curare was injected intravenously into the mother, still in apnea from her first dose. The pup continued to squirm and cry for 10 minutes, at which time the cord was cut. After the delivery and while the mother was still in apnea, the administration of ergotrate produced normal contraction of the uterine muscle. The mother recovered with no ill effects from the curare. During a second cesarean section performed in a similar manner, 4 milligrams of curare were injected into the umbilical vein of a lively, breathing pup while it was still attached to the placenta, causing complete apnea in 15 seconds. The pup could not be intubated because of the minute size of the larynx and controlled respiration by squeezing the chest was carried on for about 1 hour. After 45 minutes a few diaphragmatic contractions were felt, but a little

TABLE I

Dog	Weight Kilograms	Premedication	Dose of curare grams	Period of injection minutes	Supportive therapy	Spontaneous respiration	Duration of experiment	Condition at end	Postmortem findings	Probable cause of death
132	13	M/03 A/0006	4 (200 c.c.)	205	1200 c.c. 5% glucose 20 c.c. 50% glucose Ephedrine 1 minim intravenously	After 42 hr.	55 hr. 30 min.	Dead	Negative	Upset of electrolyte balance after long period of controlled respiration and inefficient supportive therapy
22	10.2	M/03 A/0006	1 (50 c.c.)	55	450 c.c. 5% D/W 10 c.c. 50% D/W 200 NSS	None	6 hr. 55 min.	Dead	Pulmonary edema	Too much fluid intravenously
25	10.8	M/03 A/0006	4 (200 c.c.)	185	500 c.c. 5% D/W 10 c.c. 50% D/W 200 NSS	None	8 hr. 45 min.	Dead		Too much fluid intravenously
26	11.0	M/03 A/0006	1 (50 c.c.)	70	100 c.c. amigen (by stomach tube) 70 c.c. H_2O (tube)	After 11 hr. 45 min.	15 hr. 15 min.	Alive		Now alive and well. Delivered pups 1 month later.
27	10.4	M/03 A/0006	4 (200 c.c.)	190	65 c.c. amigen (by stomach tube) 50 c.c. H_2O (tube)	None	11 hr. 25 min.	Dead	Massive cbllapse left lung.	Not turned frequently enough. On left side for last 3 hours.

M..morphine sulfate
A..atropine

later the heart stopped. Postmortem examination showed hemorrhages into the heart muscle. It is probable that our attempts at resuscitation were too rough.

We conclude from this experiment that in dogs curare does not pass the placental barriers or paralyze the uterine musculature.

In an attempt to determine the relation between the apneic dose and the lethal dose of curare, 5 dogs were given massive quantities in a short period of time by means of slow intravenous drip. Controlled respiration with oxygen through an endotracheal tube was instituted and the dogs were maintained in this manner until they either recovered or died. The results are listed in Table I. One animal survived after the administration of 1 gram (25 times the apneic dose) of curare. One dog which received 4 grams of curare breathed spontaneously after 42 hours in apnea, though it died after 55½ hours. The postmortem findings (including microscopic sections) were negative in all cases except those in which too much fluid was given or controlled respiration was improperly carried out. In contrast to Cole's conclusions in his article on the lethal dose of curare, these findings lead us to believe that curare has no specific toxicity and that these deaths were due to failure to maintain normal metabolism. The only positive finding which might be attributed to curare is the anuria that occurred in the first animal, which possibly was due to a fall in blood pressure.

CLINICAL USE OF CURARE

After we had satisfied ourselves that doses of curare which produce apnea are harmless provided the anesthetist cares for the patient properly, the administration of apneic doses of the drug to humans was begun. The technique as finally developed is as follows:

Induction. The patient is heavily medicated with a short-acting barbiturate, morphine and scopolamine, nitrous oxide and oxygen are administered with a face mask, and the anesthetist's ability to inflate the lungs is tested by pressure on the breathing bag. An apneic dose of curare, usually 200 milligrams in adults, is injected intravenously. Artificial respiration is instituted with the mask and bag when apnea develops. When the patient has reached a maximum state of relaxation, after approximately 5 minutes, an orotracheal tube with an inflatable cuff is inserted and connected to a canister of soda lime and a breathing bag. Anesthesia is continued with the concentration of nitrous oxide and oxygen, which has been previously found to keep the patient well anesthetized and well oxygenated. A Luer of curare is connected by means of a 3 way stopcock to a continuous intravenous drip inserted in a wrist vein in convenient reach of the anesthetist.

For use with children this technique has been varied somewhat, as described in detail elsewhere (6). Briefly, the procedure consists of premedication with morphine and scopola-

TABLE II.—TYPE OF OPERATION

	Curare-nitrous-oxide		All other agents	
	Cases	Per cent	Cases	Per cent
Intrapleural	106	60.5	41	23.4
Intra-abdominal	64	36.6	127	72.5
Miscellaneous	6	3.4	7	4

mine, basal narcosis with tribromethonal (avertin), intubation with cyclopropane, and maintenance of anesthesia with a high flow of nitrous oxide and oxygen in an open system. Apnea is produced and maintained with repeated doses of 30 to 40 milligrams of curare during the time the chest is open.

Maintenance. Some adult patients will resume spontaneous respiration before the chest is entered. If the respirations are sufficiently deep to provide adequate inflation of the lungs, the patient is allowed to breathe spontaneously until the pleura is opened. After that, curare is added in 20 to 40 milligram increments as necessary to produce and maintain respiratory arrest as long as the pleural cavity is open. In a completely curarized patient the usual signs of light anesthesia are masked by the muscular paralysis. Diaphragmatic contractions, slight muscular twitching, movement of the facial muscles, or a rise in blood pressure indicate too light a plane of anesthesia and the need for an additional dose of morphine, preferably administered intramuscularly.

Terminating the anesthetic. When the surgeon has effected an airtight closure of the pleura, or closure of the peritoneum in abdominal cases, pressure on the breathing bag is discontinued and the patient is allowed to build up carbon dioxide in his blood stream. If spontaneous respiration is not resumed by the time slight cyanosis occurs, controlled respiration is again instituted. This routine is repeated every few minutes until the patient breathes spontaneously. He is then allowed to breathe for himself, but until the intercostal muscles are functioning adequately, an occasional squeeze of the breathing bag is given in order to prevent the upper lobes from becoming atelectatic.

When the anesthetist is satisfied that intercostal activity has returned sufficiently and it is desired to terminate the anesthetic, the breathing bag is emptied and filled with air. The lungs are then manually inflated several times with air, after which the breathing bag

TABLE III.—COMPLICATIONS DURING SURGERY

	Curare-nitrous-oxide		All other agents	
	Cases	Per cent	Cases	Per cent
Pulse rise of over 20	42	24.0	88	50.2
Blood pressure fall to below 80	24	13.7	63	36.0
Cardiac arrest during operation with recovery	2	1.1	2	1.1
In shock at end of operation	5	2.9	19	10.9
Died during operation	4	2.3	1	0.6

TABLE IV.—POSTOPERATIVE COMPLICATIONS

	Curare-nitrous-oxide		All other agents	
	Cases	Per cent	Cases	Per cent
Pulmonary	93	53.0	91	52.0
Circulatory	66	37.7	84	48.0
Miscellaneous	86	54.8	144	82.2

TABLE V.—INCIDENCE OF COMPLICATIONS

	Curare-nitrous-oxide		All other agents	
	Cases	Per cent	Cases	Per cent
Pulmonary				
Cough	53	30.2	34	19.4
Obstruction	1	0.5	1	0.5
Laryngitis	9	5.1	8	4.5
Atelectasis	17	9.7	19	10.8
Pneumonia	7	4.0	12	6.8
Empyema	0	0.0	9	5.1
Pulmonary embolus	2	1.1	5	2.8
Subcutaneous emphysema	4	2.2	3	1.7
Circulatory				
Tachycardia	57	32.5	43	24.6
Arrhythmia	6	3.4	8	4.5
Hemorrhage	0	0.0	3	1.7
Shock	3	1.7	22	12.5
Decompensation	0	0.0	6	3.4
Coronary insufficiency	0	0.0	2	1.1
Gastrointestinal				
Emesis	43	24.6	48	27.4
Distention	20	11.4	28	16.0
Hematemesis	0	0.0	2	1.1
Hepatitis	0	0.0	1	0.5
Peritonitis	0	0.0	3	1.7
Bowel obstruction	0	0.0	7	4.0
Nervous				
Irrational	4	2.2	6	3.4
Headache	3	1.7	13	7.4
Peripheral neuritis	1	0.5	4	2.2
Genitourinary				
Retention	15	8.5	4	2.2
Hematuria	0	0.0	4	2.2
Pyelitis	0	0.0	1	0.5
Cystitis	5	2.8	4	2.2
Oliguria	1	0.5	4	2.2
Uremia	0	0.0	3	1.7
Miscellaneous				
Mediastinitis	1	0.5	0	0.0
Wound infection	3	1.7	12	6.8

TABLE VI.

	Curare-nitrous-oxide Cases	Per cent	All other agents Cases	Per cent
Average day of ambulation.	3.27		7.02	
Average day of discharge...	14.38		19.41	
Mortality in 175 cases.....	12	6.9	12	6.9

is disconnected from the endotracheal tube. Secretions are aspirated from the patient's tracheobronchial tree by means of a suction catheter inserted through the endotracheal tube. Secretions are similarly aspirated from the oropharynx and the endotracheal tube is removed. If the intercostal muscles have not recovered their power of contraction by the time the operation is ended, the anesthetic is stopped and the patient's lungs are inflated rhythmically with oxygen or a mixture of air and oxygen. The endotracheal tube should under no circumstances be removed or the patient returned to the ward until the anesthetist is satisfied that the intercostal muscles are contracting vigorously. If this rule is disregarded the patient will almost invariably develop atelectasis. Prostigmine has proved to be ineffective in our hands in hastening the return of intercostal muscle contraction.

The patient is usually awake and able to answer questions before leaving the operating table, even after operations 6 hours or more in duration. However, it must be remembered that residual muscular weakness persists for several hours and makes careful aftertreatment necessary. The patient should be placed in bed on the side operated upon and turned frequently. Coughing and deep breathing should be encouraged. Oropharyngeal oxygen should be given if indicated by the presence of dyspnea, rapid pulse, or cyanosis.

This technique has been followed throughout the entire series of cases, whether or not the operation was intrapleural, in order to build as large a uniform series as possible for statistical purposes. It has proved extremely satisfactory in intrathoracic cases. Tables II to VII present a statistical comparison of the course during and after surgery of 175 patients anesthetized with nitrous oxide and given apneic doses of curare, and an equal number of patients anesthetized for similar surgical procedures with ether, cyclopropane, and spinal analgesia.

TABLE VII.

	Curare-nitrous-oxide	All other agents
Age		
Average.....	43.7 years	47.1 years
Oldest.....	76 years	76 years
Youngest.....	16 mo.	6 days
Duration of operation		
Average.....	4 hrs. 50 min.	4 hrs. 4 min.
Longest.....	10 hrs. 40 min.	9 hrs. 35 min.
Shortest.....	10 min.	1 hour
Dose of curare in milligrams		
Average.....	283.98	
Greatest.....	790	
Least.....	20	

Advantages. The administration of curare with nitrous oxide anesthesia allows the use of the cautery inside the pleural cavity while the patient's respirations can be controlled by the anesthetist. It produces profound relaxation of the abdominal muscles. However, this can be obtained by other anesthetic agents if properly used. The patients receiving this type of anesthesia remain in very good condition during surgery and have fewer postoperative complications than those receiving other types of anesthesia. On the average the patients who received curare and nitrous oxide were ambulated earlier and were discharged from the hospital earlier than those in the control group.

Disadvantages. After curare is once administered, the signs of anesthesia are completely masked by the muscular paralysis. During abdominal operations there have occurred sudden unpredictable bouts of strong diaphragmatic contractions which are very disturbing to the surgeons. The contractions resemble hiccough, but they may well be attempts at vomiting due to too light anesthesia masked by muscular paralysis. Curare is given intravenously, which necessitates extra equipment and personnel to set it up, and its administration may be difficult in patients with poor veins. This technique requires the use of an endotracheal tube in every patient. In order to be a safe procedure it must be used only by well trained anesthetists.

TABLE VIII.—LIVER AND KIDNEY FUNCTION

	Average, preoperative	Average, postoperative
Intravenous hippuric acid—		
50 cases.....	1.04	0.89
Phenolsulfonphthalein—		
44 cases.....	75.6%	75.9%

CLINICAL RESEARCH

Considerable experimental work has been carried out on these patients who received large quantities of curare.

Blood pressure. It was found that the rapid injection of an apneic dose of curare (200 mgm.) to an anesthetized patient was often followed by an immediate and transient fall in blood pressure. Unless the pressure was taken within the first 5 minutes after the injection, this fall was missed, since the pressure rose rapidly to the precurare level.

Electrocardiograms. Electrocardiograms were taken on 30 patients during nitrous oxide anesthesia just before and about 10 minutes after the injection of 200 milligrams of curare. The cardiograms after curare showed no significant changes from those with nitrous oxide and oxygen alone. In 5 cases there was a slight lowering of the *T* waves after curare which the cardiologists considered of no significance. It was suggested that what slight variations occurred were probably due to a change in the position of the diaphragm after it was paralyzed by curare.

Liver and kidney function. The liver function was tested before and after curare in 50 cases. In most cases there was a slight decrease in liver function postoperatively. The fact that these patients had many other things done to them, such as long major surgical procedures, beside the administration of curare, makes the significance of this change questionable. There was no significant change in kidney function postoperatively (Table VIII).

Blood sugar. Blood sugar determinations were made on 4 patients before and after the administration of curare. The blood sugar rise in these anesthetized patients was minimal, averaging 13 milligrams per cent. This fact raises the question as to whether the much greater rise in the unanesthetized dogs may be a psychic phenomenon secondary to a rise in adrenalin.

Consciousness. Although we do not consider it a particularly important point, we have been interested in whether or not the injection of apneic doses of curare causes loss of consciousness. One of our patients distinctly remembered being draped for an intrathoracic operation while she was in apnea from curare. The towel clips in her skin caused no pain. This may be because she was receiving nitrous oxide and oxygen enough for analgesia, but apparently not enough to cause loss of consciousness. If the inhalation anesthesia is stopped during an operation on a patient who is apneic from curare, he will squirm and move his facial muscles. We have heard on good authority of 2 patients who received apneic doses of curare, 1 for an operation and 1 simply for experimental purposes, who were conscious and remembered it afterward. In both cases the patients suffered intense mental discomfort from their complete helplessness and inability to communicate with those around them. It is for this reason that we have hesitated to administer apneic doses to a conscious person.

With small doses up to 100 milligrams which produce muscular relaxation without respiratory paralysis, there is no loss of consciousness or analgesia whatsoever. We have tested this in 3 unanesthetized patients to whom curare was administered for relief of muscle spasm.

Some anesthetists (7, 8) are using large doses of curare without any anesthetic agent for "anesthesia" during major surgical operations. The patients seem to have no memory of the procedure. According to the reports, much larger quantities of curare are necessary to keep these patients relaxed than we have needed in patients anesthetized with nitrous oxide.

Action on smooth muscle. The action of curare on smooth muscle is still relatively unknown. We have confirmed the report of Gross and Cullen of dilatation and atony of the intestine following the administration of a large dose of curare, and the fact that the administration of morphine will prevent this dilatation of the intestine.

Placental transmission and action on uterine muscle. Although we hesitate to report an isolated case, the results in this instance parallel so exactly the findings in dogs that we feel they should be included.

A hysterotomy and sterilization with curare-nitrous oxide anesthesia were performed on a 19 year old epileptic girl 4½ months preg-

nant. A single dose of 200 milligrams of curare was administered 5 minutes after the nitrous oxide anesthesia was begun. The baby was delivered 40 minutes after the administration of curare, and when the patient had been in apnea for 35 minutes. The baby was too small to make any respiratory efforts, but all its normal reflexes (withdrawal, knee jerks, etc.,) were present and as active as could be expected in a normal fetus of that size. The mother's uterine muscle contracted perfectly normally. The duration of the operation was 1 hour 40 minutes; the duration of apnea, 1 hour 5 minutes. The baby, of course, was not viable, but the mother made a normal recovery.

Action of prostigmine. After the administration of large amounts of curare over long periods of time, prostigmine has proved in our hands to be completely without effect. However, after a single apneic dose of curare, or after smaller doses given for muscular relaxation, prostigmine seems to overcome the muscular weakness of curare quite well.

Mortality. We believe that in no case in this series could the death of the patient be attributed to the action of curare. Two of the patients on whom thoracic operations were performed died because of inability to cough out their secretions. The surgeons suspect that continued muscular weakness from the curare was the reason. However, both patients had extensive rib resections and we believe that their difficulty lay in lack of support of the chest wall rather than muscular weakness. The fact that one died 4 days and the other 10 days following surgery would seem to confirm our opinion; in no case have we seen delayed or prolonged action of curare.

INDICATIONS FOR CURARE

Intrathoracic operations. Curare is indicated in intrathoracic operations in which the surgeon desires to use the cautery. Here the combination of nitrous oxide anesthesia and apnea from curare provides excellent operating conditions with relaxed diaphragm and quiet mediastinum and no danger of explosion.

Intra-abdominal operations. Curare is indicated in intra-abdominal operations requiring prolonged complete muscular relaxation in patients whose condition contraindicates the use of a spinal or inhalation anesthetic in a deep enough plane to produce the degree of relaxation needed. The combination of first plane inhalation anesthesia and curare administered for relaxation certainly causes less change in pulse and blood pressure than spinal or deep inhalation anesthesia for long periods of time.

Emergency. Curare is indicated in the emergency where relaxation is needed rapidly. This includes certain cases in which it becomes suddenly necessary to intubate a patient who is lightly anesthetized, when a spinal unexpectedly wears off, or when for some reason an operation which was expected to be extraperitoneal becomes intraperitoneal.

We believe that at present these are the only three indications for the use of curare in anesthesia. If it can be proved that curare does not affect the uterine muscle or pass the placental barriers in human beings, such operative deliveries as version and extraction and high forceps delivery will be added to the list. Curare should never be required for cesarean section, since no muscular relaxation is necessary for this operation.

PREREQUISITES FOR PROPER ADMINISTRATION OF CURARE

We believe that curare is completely harmless when used by one who has sufficient understanding of its action and of human physiology to give adequate care to the patient under the influence of the drug. In the hands of technician anesthetists ignorant of its physiologic effects, who use curare because of inability to produce muscular relaxation by inhalation anesthesia, it is dangerous.

We believe that the anesthetist who is to administer curare, at least for intrathoracic cases, should fulfill the following requirements:

First, he should have a thorough knowledge of respiratory physiology and all the changes that can take place during controlled respiration, of the changes when a lung is nonfunctioning with or without its circulation intact, and of how to protect normal lung tissue from contamination by secretions from diseased portions.

Second, he must be able to give good inhalation anesthesia. He must be able to relax pa-

tients with ether and cyclopropane and to give good nitrous oxide anesthesia without any hypoxia.

Third, we feel that every person planning to use curare in anesthesia should learn its action without anesthesia by administering it to unanesthetized dogs. Only in this way can the differentiation between the signs of too light anesthesia and too little curare be learned.

It is of the utmost importance that anesthetists using curare be thoroughly convinced that although the diaphragm has recovered its power of contraction and the patient may be able to oxygenate himself well, he will die of atelectasis if controlled respiration is stopped before the intercostals have recovered. This is most forcibly impressed on an anesthetist by allowing him to curarize and maintain a few dogs alone. Sooner or later he will kill one in this manner. The postmortem findings are typical and striking. The lesson is never forgotten.

The importance of postoperative care must also be stressed. Frequent turning of the patient, encouraging the patient to breathe deeply and cough, and in thoracic cases the proper use of oxygen are essential.

The safe use of curare depends entirely upon the knowledge of the anesthetist administering it. Its action and physiological effects should be studied by everyone who plans to use it.

CONCLUSIONS

1. The use of curare in apneic doses is a safe procedure in the hands of a competent anesthetist. Its safety depends entirely upon the knowledge of the anesthetist administering the drug.

2. The uterine muscle is probably unaffected by curare.

3. Curare probably does not pass through the placenta.

4. No antidotes are of any value after the administration of large doses of curare except efficient artificial respiration until the intercostal muscles are contracting strongly.

5. Curare has no delayed action or prolonged action when administered intravenously.

6. The advantages of the use of curare with nitrous oxide anesthesia are: (a) It allows the use of the cautery inside the pleural cavity while the patient's respirations can be controlled by the anesthetist. (b) It produces profound relaxation of the abdominal muscles for long periods of time with less change in pulse and blood pressure than other anesthetics. (c) The condition of the patient receiving this type of anesthesia remains good during surgery. (d) Fewer postoperative complications occur than with other types of anesthesia.

7. The disadvantages of this technique are: (a) In order to be a safe procedure it must be used only by well trained anesthetists. (b) Since the curare is administered intravenously, extra equipment and hands are necessary. (c) It is necessary to use an endotracheal tube in every patient.

8. Further investigation is needed on the following points: (a) lethal dose; (b) action on uterine muscle and passage through placenta in human beings; (c) production of unconsciousness or analgesia or both.

SUMMARY

A series of experiments in the administration of curare to unanesthetized dogs in doses of from 40 milligrams to 4 grams (2 to 200 c.c.) is reported.

A series of 175 cases in which apneic doses of curare were administered to patients undergoing major surgical procedures with nitrous oxide anesthesia is reported and compared with a similar series of cases in which other types of anesthesia were used.

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PREINFUSION—A STUDY IN THE PREVENTION OF HEMORRHAGIC SHOCK

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THE best treatment of shock is its prevention, for shock is more easily prevented than treated. This is the consensus of most workers who have studied shock in man or animal. We had noticed earlier that dehydrated animals succumbed to hemorrhagic shock sooner than well hydrated animals, and that they tolerated concentrated plasma or albumin solutions less than well hydrated animals (13). This observation led to our present work. We have attempted during the last 2 years to prevent hemorrhagic shock in dogs either by preinfusion or by increasing the quantity of fluid reinfused during experiments with graded repeated hemorrhages. No systematic study on this problem was known to us until our work was completed, when Ingraham and Wiggers reported "fluid priming" with saline solution as having a favorable effect in hemorrhagic shock in dogs. Prinzmetal and collaborators mention briefly that saline solution given to mice prior to scalding decreased mortality.

Surgeons have long recognized that dehydrated patients are poor operative risks, and preoperative infusions and infusions during severe operations are being used widely. We are concerned here only in this part of preoperative care, but we want to stress the importance of an adequate plasma albumin level as an important factor in the retention in the circulation of infused sodium chloride solution. At the same time, particular care must be exercised in the calculation of the amount of infusion fluid, because the patient may suffer from an excess of fluid infusion. Patients may appear normal clinically before operation but yet may go into shock easily. This may be due to lack of fluid reserves or to a condition of impending shock, where disease may have depleted reserves and diminished the resistance of the patient. Yet, blood pressure and pulse and most other determinations may yield normal values. Estimation of the blood volume and of the thiocyanate space may reveal a deficiency, but these tests are difficult and normal standards and deviations are equivocal. For this reason, the value of a preinfusion should be weighed for every patient on whom a major operation is planned.

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METHODS

The method employed for the production of hemorrhagic shock in the unanesthetized dog has been described previously (1). In short, it consists in the hourly withdrawal of 25, 23, 21, 19, and 17 per cent of the measured blood volume, and of the reinfusion of the amounts withdrawn (minus 2 per cent of each hemorrhage which is used for determinations) after an interval of 30 minutes between bleeding and reinfusion. The condition of the animals with regard to resistance to shock could be estimated by determining the arterial carbon dioxide content 30 minutes after the first hemorrhage. These "critical" carbon dioxide values permitted the prediction of the period of survival and the grouping of the animals according to their resistance to the experimental procedure.

In the present work the following modifications of the graded hemorrhage were employed in different groups of animals. (A) Preinfusion of an amount of fluid equivalent to 15 percent of the control plasma volume. The duration of the preinfusion was 30 minutes. In one group of animals the first hemorrhage was performed 5 minutes after the end of the preinfusion, and in another group the first hemorrhage was performed 2 hours after the preinfusion. (B) Infusion of an amount of fluid equivalent to 15 percent of the con-

TABLE I.—EFFECT OF PREINFUSION WITH SALINE OR WITH GELATIN ON THE CRITICAL ARTERIAL PLASMA CARBON DIOXIDE OF DOGS SUBJECTED TO ONE HEMORRHAGE OF 25 PER CENT OF THEIR BLOOD VOLUME

No. of Dogs	Procedure	Per cent of dogs with a critical arterial plasma CO_2 of		
		Below 20	20–29.5	30 and above
215	All controls	27	49	24
41	Control subgroup 1	29	44	27
15	Control subgroup 2	13	67	20
12	Control subgroup 3	33	42	25
	Preinfusions given before first hemorrhage			
26	Saline 5 minutes before	19	27	54
25	Gelatin 5 minutes before	0	44	56
16	Saline 2 hours before	13	56	31
17	Gelatin 2 hours before	0	47	53

trol plasma volume in addition to the 23 per cent routinely administered at the time of the first reinfusion. The preinfusion fluid or the additional fluid infused were either saline solution 0.9 per cent, or gelatin solution. The gelatin employed was pigskin gelatin specially manufactured for biological use, 8 per cent in 0.9 per cent saline, adjusted to *p*H 7. The gelatin solution was sterile, pyrogen free, and nontoxic. Blood pressures were recorded continually from one carotid artery. Blood was withdrawn from one cannulated femoral artery. The following determinations were performed: During the control period and following the last (5th) hemorrhage, plasma volume, hematocrit, hemoglobin, sedimentation rate, total plasma proteins (including gelatin), albumin and globulin, and arterial plasma carbon dioxide content. Arterial plasma carbon dioxide content was determined also 30 minutes after each hemorrhage, and 30 minutes after each reinfusion. The methods employed in these determinations have been described (11, 17).

The effectiveness of the preinfusion or of the larger first reinfusion were determined by comparing survival times and "critical" carbon dioxide values with the corresponding data of control experiments with simple graded hemorrhage, as described above. Control experiments were repeated regularly during the presently reported series of experiments in order to rule out seasonal or other variations. All data were treated statistically[1] by the chi square test, by the T test (7) or by the u-test (22), and when the differences are called significant in this paper, it means that they were statistically significant as indicated by these tests.

RESULTS

A. Preinfusion. In Table I the effect of preinfusions on the "critical" carbon dioxide values are compared with the "critical" carbon dioxide values in 215 control animals not receiving a preinfusion. The control subgroups 1 to 3 in Table I are unselected groups of control animals used consecutively, but each group of experiments was performed at different times of the year. The size of each group was of the order of magnitude of the groups that received preinfusions. The distribution of the critical carbon dioxide values in the 3 smaller control groups did not differ statistically from the distribution obtained in the total control group of 215 animals.

We have presented evidence (1), that the arterial plasma carbon dioxide values, taken ½ hour after a rapid hemorrhage of 25 per cent of the measured blood volume can be used to predict the resistance of the animal to further hemorrhages and to judge the effectiveness of blood or plasma substitutes. The lower this "critical" carbon dioxide, the less resistant the dog will be to further hemorrhage or to substitution therapy. Comparing the distribution of carbon dioxide values in the control group with those of all preinfusion groups, it is evident that a shift of distribution to the right, i.e. a greater incidence of higher carbon dioxide values, has occurred. This is particularly true and significant in the case of the gelatin preinfusions 5 minutes or 2 hours before the first hemorrhage. Saline preinfusion was significantly effective only when given 5 minutes before hemorrhage, but not, when given 2 hours before the hemorrhage.

The higher plasma carbon dioxide values following preinfusions signified that the prob-

[1]By Dr. H. Silverstone, Department of Cancer Research of Michael Reese Hospital.

ability of survival would be increased. However, it was considered possible that some of the fluids given as preinfusions might produce only a temporary rise of the carbon dioxide, which thus might not truly indicate actual survival, as established by the control experiments. In order to answer this question, we have tabulated our experiments according to the length of survival in Table II. The experiments with 5 hemorrhages and 5 reinfusions lasted 5 hours, including the preliminary control period. Thus, "died during the experiment" denotes death between 1 and 4½ hours after the first hemorrhage. "Died during the night" denotes that the animal died between 3 and 15 hours after the termination of the experiment. "Survived +24 hours" denotes that the animal lived 24 hours or more after the termination of the experiment. In general, the latter group of animals survived indefinitely, and most of those that died, succumbed to pneumonia or to other diseases that had no direct relation to the experiment. In some animals an early infectious process like distemper may have been present before the experiment.

The control group of 41 dogs did not receive a preinfusion, and was subjected to the standard procedure of repeated hemorrhage and reinfusion of their own blood, as described above under "Methods." Preinfusion with 0.9 per cent saline 2 hours before the first hemorrhage did not benefit the animals at all, but preinfusion with saline solution 5 minutes before the first hemorrhage increased survival through the experimental period somewhat. Preinfusion with gelatin solution, administered 5 minutes before the first hemorrhage, significantly increased ultimate survival. Preinfusion with gelatin, given 2 hours before the first hemorrhage, did not increase ultimate survival, but increased survival through the experimental period.

Animals which, ½ hour after the first hemorrhage, have plasma carbon dioxide values of 20 volumes per cent and below have very little probability of survival under the conditions of our control experiments, than those with carbon dioxide values above 20 volumes per cent. The percentage of dogs with carbon dioxide values above 20 per cent (shown in brackets in Table II) was greater in those animals that received preinfusions, than in the controls. Seventy-one per cent of the 41 control dogs of Table II have carbon dioxide values above 20 volumes per cent. When preinfusions had been given, the following changes were observed: 85 per cent of the 26 dogs preinfused with saline solution 5 minutes and 87 per cent of the 16 dogs preinfused with saline 2 hours before the first hemorrhage, had carbon dioxide values above 20 volumes per cent. The corresponding values were 100 per cent of all dogs preinfused with gelatin 5 minutes or 2 hours before the first hemorrhage.

TABLE II.—EFFECT OF PREINFUSION WITH SALINE OR WITH GELATIN ON SURVIVAL OF DOGS SUBJECTED TO GRADED HEMORRHAGE AND REINFUSION WITH THEIR OWN BLOOD

No. of Dogs	Procedure	Per cent of dogs that		
		Died		Survived +24 hours
		During experiment	During night	
41 (71)*	Control	44	20	36
	Preinfusions given before first hemorrhage			
26 (85)	Saline 5 minutes before	36	16	48
25 (100)	Gelatin 5 minutes before	24	16	60
16 (87)	Saline 2 hours before	25	50	25
17 (100)	Gelatin 2 hours before	18	35	47

( )*Per cent of dogs with plasma carbon dioxide values above 20 volumes per cent.

Corresponding to the tendency to elevate the carbon dioxide value, the preinfusion tended to increase the survival time of the experimental animal.

B. Additional infusion. In the preceding experiments, preinfusion was given before the first (critical) hemorrhage and before the "critical" posthemorrhage carbon dioxide determination had been performed. Therefore, the effect of such preinfusion on the resultant "critical" carbon dioxide values could be indirectly determined only by comparison with expectancy in normal controls, as explained above. In order to evaluate the effect of infusion on the survival of dogs with a known "critical" carbon dioxide level, uninfluenced by previous infusions, a different procedure

was designed. Dogs were subjected to the first hemorrhage, and the "critical" carbon dioxide was determined. Then, at the time of the first reinfusion, a volume of 8 per cent gelatin solution, amounting to 15 per cent of the measured control plasma volume, was given in addition to the returned 23 per cent of the dog's own blood. In order to test the value of this procedure rigidly, only animals with a "critical" carbon dioxide below 20 volumes per cent were used. The control and the experimental group contained 16 dogs each. The mean survival time of the animals that died in less than 24 hours was 4.2 ± 1.1 hours for the control group, and 7.2 ± 1.2 hours for the experimental group. Only 4 animals of the control group and 6 animals of the group with additional infusion survived the experimental period of 4½ hours. The difference between these values approaches significant difference. In view of this it is believed that additional infusion may have some value. We did not find a significant increase in indefinite survival by this procedure. As already explained, the probability of survival of animals with low arterial posthemorrhage plasma carbon dioxide values is small, and possibly experimental conditions in these experiments were too severe. The mean carbon dioxide values following the second hemorrhage were significantly higher than those following the first hemorrhage in the animals which received the additional infusion, while those of the control group were lower.

DISCUSSION AND CONCLUSIONS

While we feel that we have demonstrated the usefulness of preinfusion, we want to stress that we do not advocate indiscriminate or excessive use of infusions before or during operations. Others have covered the field of water balance adequately, and we refer to their papers (2–6, 8, 15, 16, 18, 21). Our results indicate, also, that in the case of persons exposed to the dangers of shock proper water reserves are essential. If a surgical patient has lost blood or excessive body fluid before operation, or if a seriously sick patient is in impending shock or already in shock before operation, he must be treated according to the estimated or measured losses of fluid, hemoglobin, plasma proteins, and salts, and does not fall into the category of preinfusion cases. In the preparation of surgical patients for major operations, most surgeons use 0.9 per cent saline, or 5 per cent glucose, or a mixture of both. If our experience in the dog can be applied to the human, gelatin solution can be recommended as superior to the crystalline solutions. This is especially true, when the solutions are given up to 2 hours before operation. It is generally agreed that crystalloid solutions rapidly leave the circulation of an animal in shock (8), and we have confirmed this earlier in our work (14). In normal man, infused saline solution cannot be found in the circulation approximately 2 hours after infusion (9). When there is an increased permeability of the capillaries or when the plasma proteins fall below a critical level, saline is especially contraindicated as an infusion fluid. Infusion of an excessive amount of saline not only tends to produce edema in a patient with a critically low albumin level, but it also further depletes the plasma proteins by washing them out into the tissue spaces as the saline rapidly leaves the circulation (2). In our experience, infusing gelatin solutions to nephrotic patients with a marked edema and a critically low albumin level at times was followed by diuresis and reduction of edema. Gelatin solutions never were found to produce edema in man or in the dog.

It would seem practical therefore, to recommend the use of gelatin as preinfusion fluid before operations, and as infusion fluid during operations, beginning the preinfusion only shortly before operation. In our previous work (12) and in present work under publication, we have gained the impression that in man and in the dog, the preparation of gelatin used was harmless even in large amounts. We have not used regularly repeated massive injections of gelatin, however, and it may be, that difference of opinion with regard to noxious effects of gelatin infusion may be related to this factor, in combination with the brand of gelatin employed (20). We have used a volume of 15 per cent of the measured plasma volume for preinfusion. This amount was found by experimentation to be optimal when infused over a 30 minute period. It

seems reasonable to assume that, in case of man, 15 per cent of the plasma volume may be taken as a starting point for the establishment of the amount of preinfusion to be used routinely. Thus, in a person weighing 60 kilograms, assuming a blood volume of 1/13th of the body weight, a total blood volume of 4.62 liters, and a plasma volume (assuming a hematocrit value of 45) of 2.54 liters are calculated. A preinfusion of 15 per cent of the plasma volume would constitute 381 cubic centimeters of a gelatin solution. This is not a large volume and we know that some surgeons use much larger volumes of saline or saline-glucose solution, preoperatively. However, some give the solutions subcutaneously, and we have no experimental results to discuss this. We can state, however, that the practice of giving solutions 12 hours in advance of an operation, as used by some surgeons, does not offer any advantage in the light of our results on the dog. We have found, that gelatin solutions, due to their colloidal properties, stay in the circulation for longer periods of time than do crystalline solutions, and that therefore, smaller volumes of gelatin than of crystalline solution may be infused in the preoperative patient.

We want to suggest that gelatin solution for preinfusion, or for infusion during operation, is better than saline or glucose infusion, but not better than infusion of blood or plasma. However, where economic considerations or expediency of administration plays a rôle, as in emergency accident cases, we have used gelatin solutions extensively, supplemented occasionally by packed red cells, and have had gratifying results.

SUMMARY

Preinfusions of saline solution 0.9 per cent, or of gelatin solution 8 per cent, given immediately before the first of a series of graded hemorrhages and reinfusions in the dog, increased significantly the mean "critical" plasma carbon dioxide values, 30 minutes after the first hemorrhage. Survival times were prolonged significantly by the gelatin solution but not by the saline solution.

In the case of preinfusions given 2 hours before the first hemorrhage, only the gelatin solutions were found beneficial in raising plasma carbon dioxide values and prolonging survival times.

When dogs with low "critical" plasma carbon dioxide values were reinfused with their own blood plus an extra volume of gelatin solution, their survival times were prolonged.

The application of the data to the surgical patient is discussed.

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EDITORIALS

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CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEOESOPHAGEAL FISTULA

THE last decade has witnessed the inclusion of several types of intrathoracic anomalies in the realm of congenital lesions amenable to surgical correction. Among these are certain malformations of the esophagus, heart, and great vessels. The most frequent type of esophageal anomaly occurs in a characteristic form in approximately 90 per cent of the cases. This form consists of an atresia of the esophagus at a level corresponding to the junction of its upper and middle thirds; in addition, there is a fistulous communication between the trachea and the upper end of the lower esophageal segment. Recognized by Gibson two hundred and fifty years ago, the lesion resisted surgical correction until 1939, when Leven and Ladd independently and almost simultaneously employed similar techniques and successfully circumvented the anomaly by a multiple stage operation consisting of gastrostomy, ligation and division of the tracheoesophageal fistula, and cervical esophagostomy. This procedure proved to be life-saving although it presented the additional problem of an eventual antethoracic esophagoplasty. Two years later the reconstruction of intrathoracic esophageal continuity by means of a single stage operation was successfully accomplished; this procedure has proved to be practicable and more satisfactory than has any other for a large majority of the cases for which surgical correction is undertaken.

With the realization that surgical correction offers considerable promise of cure, there has been an awakening of interest in the diagnosis of the anomaly. Even so, the period of time has been so short since surgical correction became available that the true incidence of the anomaly has not as yet been determined. It is known, however, that among the residents of the relatively small county in which the author resides, eight cases have been verified in the last eleven years, an incidence rate of one in 2,196 newborn infants.

The diagnosis of the typical form of the anomaly presents no great difficulty, as the atresia of the upper esophagus can be readily determined by the failure of a catheter to pass into the stomach. As the remote possibility of a partial esophageal obstruction with a diameter less than that of the catheter must be excluded, the completeness of the obstruction can be determined by roentgenography following the ingestion of iodized oil. In the presence of a complete esophageal obstruction, the finding of air in the gastrointestinal tract

is indicative of a fistulous communication between the trachea and the lower esophageal segment.

The most frequent variation of the anomaly consists of an esophageal atresia without air in the gastrointestinal tract. The failure of air to enter the stomach is due to a tracheoesophageal fistula of smaller than average size or more commonly to a rudimentary lower esophagus which does not communicate with the trachea. Tracheoscopy is helpful in such cases in order to determine whether a fistula is present or absent. A considerably less frequent variation consists of the typical anomaly with an additional fistula between the proximal esophagus and trachea. The superior fistula in this instance can be recognized by roentgen examination with ingested iodized oil or by endoscopy. Tracheoesophageal fistula unassociated with atresia is also infrequent; the diagnosis is not evident from the passage of a catheter since the esophagus is patent, but is readily apparent on endoscopy or on roentgen examination with iodized oil with the patient in a prone position.

The important factors in the evaluation of operability are the size and general condition of the patient and the presence of any other anomalies. The incidence of prematurity in infants with esophageal atresia is considerably greater than in normal infants; those premature by more than three or four weeks and whose weight is less than four and a half pounds have in general a less favorable prognosis than full-term infants of normal size. The outcome following surgical correction is particularly dubious in the listless premature infant who has a feeble cry and is unable to clear the respiratory tract of secretions. In the full-term infant, atelectasis or pneumonitis can usually be corrected, thereby presenting no contraindication to operation. Associated congenital anomalies, with the exception of a certain few of the cardiovascular system, have been infrequent and are usually compatible with life.

The most rational procedure for the correction of the typical anomaly consists of an intrathoracic restoration of esophageal continuity. This operation is preferably performed through a right-sided extrapleural approach. In spite of the small size of the infants, the exposure is entirely adequate. Division of the azygos vein is not required except in the rare instances in which the fistula enters the trachea at its bifurcation. The operation consists of transection of the lower esophagus at its junction with the trachea and closure of the opening into the trachea by suture. The lower end of the upper esophageal segment is opened to a diameter corresponding to the small diameter of the lower esophageal segment and an anastomosis is made. The practicability of this plan in a large percentage of the cases is evidenced by the fact that since 1939 an intrathoracic anastomosis has been possible in approximately 76 per cent of the forty-two patients operated upon in a clinic where intrathoracic reconstruction is attempted if at all feasible. An intrathoracic anastomosis has usually been possible when air is present in the gastrointestinal tract before operation (83.3 per cent) and it has only rarely been possible in those cases without air in the stomach or intestines (20 per cent).

There is necessarily a predisposition to leakage at the site of the anastomosis if too great tension is present or if the wall of the lower esophageal segment is unusually thin. The resultant fistula to the exterior by way of the extrapleural wound invariably heals spontaneously. Although a stricture forms at the site of the anastomosis in such cases, it is short and can be dilated successfully with a good functional result. A less frequent but more serious possibility following leakage of

the anastomosis is the recurrence of a tracheoesophageal fistula which rarely closes spontaneously and usually produces a fatal pneumonia before the condition of the wound permits an operation to repair the fistula.

If an anastomosis is impossible, the multiple stage procedure of closure of the tracheoesophageal fistula, gastrostomy, cervical esophagostomy and eventual antethoracic esophagoplasty is the only method available at present for the saving of life and for the providing of a means for swallowing. Successful instances of construction of a satisfactory antethoracic tube in such patients have recently been described by Ladd and by Lam.

The ability of newborn infants to withstand the operation of anastomosis has been surprising. Among the forty-two patients operated upon, only two deaths have occurred during operation and in both instances anomalies of the aorta were partially or wholly responsible for the deaths. Survival following operation has, as might be expected, increased considerably with improvements in surgical technique and general management. Realization that the amount of blood replacement during operation must be greater than the estimated blood loss has lessened the factor of operative shock and has provided a nutritive balance to compensate partially for the absence of feedings prior to operation. The restriction of normal physiologic saline solution to a minimal amount has almost completely prevented the postoperative generalized edema which occurred invariably in the patients treated during the developmental period of the operation. The use of penicillin locally and intramuscularly has decreased the incidence of breakdown of the anastomosis and wound sepsis. A further lessening of wound sepsis should occur with the use of other antibiotic agents for penicillin-resistant bacteria. The intravenous use of plasma and amino acids has been helpful in maintaining nitrogen balance until the time when swallowing can be undertaken through the reconstructed esophagus, in the event that gastrostomy is not used as a temporary means for feeding. Excellent nursing care is of particular importance in this type of case.

Whereas the recovery rate was low in those infants operated upon during early personal experiences with this operation, there has been a survival rate of 66.6 per cent following primary anastomosis in the nine patients operated upon during the last two years. The establishment of normal esophageal function in twelve among thirty-one patients in whom an anastomosis has been made in one clinic bears evidence of the fact that the future now holds considerable promise for infants born with esophageal atresia and for whom surgical correction has only recently become available.

CAMERON HAIGHT.

THE TRAINING OF SURGICAL RESIDENTS IN VETERANS ADMINISTRATION HOSPITALS

UNTIL about a year ago, Veterans Administration hospitals were operated on the premise that the patient would receive the best professional care by utilizing only full time graduate physicians who would perform all professional services without the aid of a house staff. Hospitals frequently were placed at great distances from medical centers and medical teaching institutions. University faculty members were called upon only when expert professional care was needed which could not be rendered by the full time Veterans' physician. No internes or residents were utilized. Little effort was made to improve the ability and knowledge of the Veterans Administration physician by enlisting the information and skill of outstanding

civilian surgeons and training institutions, and little opportunity for further training was offered him.

When General Omar Bradley assumed responsibility of the Veterans Administration and placed General Paul R. Hawley in charge of the hospital program, they realized that a change of policy would be necessary to meet the greatly increased demands placed upon Veterans' hospitals by the addition of all World War II veterans. It would have been impossible, under any circumstances, to secure the services of a sufficient number of full time physicians as Veterans Administration employees to meet existing needs alone without considering the rapidly expanding program. Therefore, they sought the co-operation of the medical schools of this country and established what is spoken of as the Deans' committee program. Under this program, those medical schools, through their deans, which are so geographically located and adequately staffed to undertake the program, have assumed responsibility for the professional care of patients, and for a resident training program in a number of Veterans Administration hospitals.

Under the supervision of Doctor Paul B. Magnuson, acting assistant medical director for Research and Education, the program has been expanded so that fifty-six class A medical schools in the country already are participating, and a large number of Veterans' hospitals are so administered.

Although individual variations in the Deans' committee programs exist in different medical schools, it is believed that the basic aims and functions are quite similar. The program now in operation at the Veterans Administration Hospital, Hines, Illinois, is fairly representative of most such programs, and a brief discussion of its operations will be presented. This discussion will be limited to the surgical division of the hospital.

In order to render the best professional care to patients and to establish a well functioning resident training program, it was necessary to establish general and specialty surgical services and attempt to place patients on services best suited to the care of their disease. After carefully analyzing figures on the admissions and duration of hospital stay of patients with varying surgical demands, it was decided that the needs of the Hospital could best be served by dividing the one thousand available surgical beds as follows: general surgery, 300; orthopedic surgery, 150; urology, 100; otolaryngology (including malignant tumors of these anatomical regions), 100; ophthalmology, 50; plastic surgery, 50; vascular surgery, 50; tumor service, 150; women's surgery, 50. Independent services in thoracic surgery and neurological surgery were established in another section of the Hospital.

It is the responsibility of the Deans' Committee representing Northwestern University, the University of Illinois, and Loyola University Colleges of Medicine to recommend the appointment of a sufficient number of attending surgeons to render the best possible professional care, and to train the residents adequately. It is required that all attending surgeons be veterans of World War II, be certified by their respective qualifying board, or have equivalent training, and be a faculty member of a participating medical school. Each surgeon must assume responsibility for the patients placed under his care, and he must spend an adequate amount of time at the Veterans Hospital to carry out his responsibilities. The great majority of surgeons spend five half days per week at the Hospital. Each one has assigned to him one or more residents and a designated number of beds, depending upon the number of patients that can satisfactorily be cared for by one surgeon and his resident staff. This varies with different special-

ties but averages about thirty beds per service.

It is the responsibility of residents assigned to clinical services to record careful histories and physical examinations and order all indicated special studies. Under the direction of the attending surgeon, the resident administers preoperative and postoperative care and assists at all operations of patients on his service. Each service has an average of two operating days per week. Most residents act as second assistants on other clinical services an additional two days per week. Thus he is given a total of four half days in the operating room and the opportunity to observe the technique of various surgeons. As we have twelve general surgical services at the Veterans Administration Hospital, Hines, Illinois, and as it is impossible for each resident to serve on all services, an effort is made to distribute the patients in such a manner that each service will get as great a variety as possible of general surgery. For this reason, we discourage the assignment of special fields of general surgery to individual services.

RESIDENT TRAINING PROGRAM

All men selected for residencies in the Veterans Administration hospitals must have served on active duty in World War II. The great demand for graduate training by returning medical officers cannot be met by existing facilities, and far more applications are received than can be favorably acted upon. Unfortunately, this denies graduate training to many men desiring it. However, it has enabled us, by careful selection, to obtain highly qualified men who are both competent and conscientious. A training program is designed to meet the requirements of the various specialty boards with such modifications as the Deans committee deems advisable. As most residents obtained some graduate training prior to or during the war, the training programs are arranged to meet the needs of the individual resident rather than to follow a prescribed course for all.

Certain fundamental requirements are incorporated in the resident program. As all of the specialty boards have recognized the importance of graduate training in the clinical application of the basic sciences, an extensive program has been arranged in these fields. Each resident spends six months in the pathological laboratories where he studies all operative specimens, and assists at, or performs, a large number of necropsies. Lectures and demonstrations in pathology are conducted daily by faculty members of the participating universities. Surgical anatomy is taught by consultants who are both qualified surgeons and anatomists. Physiology, biochemistry, and bacteriology are taught at weekly conferences throughout the entire resident period. All basic science studies are taught with emphasis upon their clinical application, and joint conferences between the clinicians and the basic science instructors are held to make these conferences as practicable as possible.

To provide residents with a thorough training in the diagnosis and principles of surgery, efforts are made not to confine training to a limited field. Those residents who are specializing in general surgery spend approximately six months on diagnostic services, including the diagnosis and treatment of malignant disease. The large number of patients admitted to this Hospital with neoplastic diseases give an excellent opportunity for this type of training. During the clinical years of the residency, approximately one year is spent on surgical specialties, as the ability to recognize and direct the proper treatment of diseases of these specialties is believed to be important.

In addition to the intimate personal training given to the residents by the attending

surgeons, a large staff of consultants are available for lectures and demonstrations in fields in which these consultants have gained renown.

Men who desire training in the special fields of surgery are first assigned to general surgical services for a varying length of time in order to teach them the principles of surgery and of surgical technique before assigning them to their chosen field.

Of nearly one hundred and thirty residents on duty at this Hospital, sixty are being trained in surgery and the surgical specialties. With similar programs in a large number of Veterans Administration hospitals being administered by Deans' committees of various medical schools, a great many World War II veterans are having opportunities for graduate training and specialization which they would otherwise be denied.

The chief function of Veterans Administration hospitals is to administer the best possible care to men who have served their country in the armed forces and who are in need of such service. The newly created program not only is offering excellent training opportunities but is providing the veteran patient with the services of the best medical talent in the country, and is rendering him the best obtainable professional care. The greater efficiency resulting in a more rapid turnover of patients is permitting existing facilities to care for a far greater number of veterans than was true in the past. CHARLES B. PUESTOW.

CORRESPONDENCE

ANTERIOR TRANSPLANTATION OF POSTERIOR DELTOID FOR SHOULDER PALSY AND DISLOCATION IN POLIOMYELITIS. —A Correction.

To the Editor: In connection with my article on the transplantation of the origin of the posterior deltoid for "Shoulder Palsy and Dislocation from Poliomyelitis," it should be pointed out that Dr. Frank R. Ober of Boston referred to this method which he had evidently used several times in "Lectures on Reconstruction Surgery of the Extremities of the American Academy of Orthopedic Surgeons, 1944." Although this reference was included in my article, specific reference to the date of Dr. Ober's publication was not available except to those readers who wished to develop the matter thoroughly through familiarity with the references included.

In a personal communication from Dr. Ober dated January 22, 1947, he states that he had performed the operation at least 12 years ago, which would antedate my performance of the operation on April 6, 1942. I feel that Dr. Ober should have clear-cut credit for prior publication of the method. My purpose in publishing this case report was to establish the permanency of the end-result and to point out the utility of the operation in the cure of recurrent paralytic dislocation of the shoulder, for which purpose it was quite effective in the case recorded.

PAUL H. HARMON, M.D.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

THE SURGICAL FORUM

OWEN H. WANGENSTEEN, M.D., F.A.C.S., Minneapolis, Minnesota

THE Forum on Fundamental Surgical Problems was instituted by the Board of Regents of the American College of Surgeons to provide an opportunity, especially to the younger surgical group, for the presentation of the results of original clinical and experimental research. The success of the undertaking appears to have been well established in its first session held in conjunction with the Clinical Congress in Boston in October, 1941. The long war years interrupted further meetings until the December, 1946, assembly of the Clinical Congress in Cleveland. The promise held out by the Boston meeting 5 years earlier for a keen interest on the part of practicing surgeons in the type of program provided for in the Surgical Forum was again demonstrated in the Cleveland sessions.

The Surgical Forum affords a large surgical audience the opportunity to become acquainted with the work of many productive clinical and experimental investigators through the medium of the concise presentation; at the same time, it accords a number of young, well trained surgeons their first opportunity of a hearing before a national surgical organization. In the past, not infrequently, young surgeons have found it necessary to have their work receive recognition before another audience before surgeons would deign to hear them. The late William J. Mayo felt keenly that the wisdom of age and experience should be exchanged freely with the enthusiasm of youth, and that both old and young would benefit by the barter. In the main, the most original contributions to surgery are made by young men. For the improvement of surgery, as well as the enlightenment of surgeons with greying hair and other marks of advancing years, it is important that young, productive workers in surgery be provided an opportunity early in their careers for active participation in surgical gatherings—before the ravages of time dampen their enthusiasm.

Furthermore, surgeons are not long the best company for one another. Surgeons need the vitalizing influence which comes from association with workers in other fields of medicine. Hence, programs constituted year after year only from the membership of a like-minded group of men, such as surgeons, are likely to reveal traces of nutritive deficiencies. No group of medical men can suffer isolation long without exhibiting unmistakable evidences of want. Recognizing the great importance to surgeons of the life-giving spirit and vital sustenance to be gained through association with fellow workers in the broad domain of medicine, the Board of Regents of the American College of Surgeons has authorized inclusion of papers of general interest to surgeons, emanating from the pens of investigators in other provinces of medicine. The interests of the membership of a large organization are served best by provision for the most original and stimulating papers that come within the scope of concern of its auditors, and that are pertinent to the occasion. It is unimportant whether the papers come from within the membership or by invitation to nonmembers. In subsequent sessions it is to be hoped that surgeons may have the opportunity of hearing similar presentations from the fruitful labors of young bacteriologists, biochemists, physiologists, and pathologists, especially in fields where the work touches the interests of the surgeon.

It is the professed purpose of the Surgical Forum to attempt to bring before its assembly

Chairman, Committee on Forum on Fundamental Surgical Problems.

each year the best that is new in surgery. Announcement of new-found knowledge of special interest to surgeons and wider dissemination of new, significant information in the interphases between surgery and allied medical specialties suggests the objectives which the sponsors of the Surgical Forum have in mind in the formulation of programs for presentation. This venture has had the hearty support of the professors of surgery in the medical schools of the American universities. If there can be realized the endeavor to bring annually to the Clinical Congress the best creative thought and original achievement in American surgery, the Surgical Forum will continue to perform a useful function. The Surgical Forum might well become the federated surgical society of America embracing, as does its preclinical prototype, a number of related specialties. There is a great need for more intimate co-ordination between the scientific programs of the various surgical specialties such as anesthesia, neurosurgery, orthopedics, plastic surgery, thoracic surgery, urologic surgery, and their parent mother, general surgery. The Surgical Forum is serving to focus important notice upon a rather large group of young men in universities who are making worth-while contributions to the progress of surgery. The sponsors of the Forum nourish the hope that this new venture will afford productive men, both young and old, through the whole range of surgery, a useful outlet for the announcement of the results of their investigations. An annual program, embracing new accomplishments in the several provinces of surgery and the most original thought, will be attractive and reciprocally advantageous to participant and auditor alike. Such a program has in it the cement substance to unify by a common bond the progressive spirit of the best in American surgery and its specialties. Realization of such an objective would infuse into our handicraft more of the scientific outlook and leave an indelible impress upon American surgery for the better.

During the long war years, the staffs of our surgical clinics were depleted and those who remained behind became absorbed in teaching and patient-care responsibilities. Now, the obligation of making the very most of their facilities available for graduate training for returned veterans is and will continue to be an important responsibility of all teaching surgical clinics. Yet, in the midst of pressing obligations of many kinds, it is eminently important that university surgical clinics enlist the interest of their young surgical aspirants in the prosecution of research. It is to new facts, the fruit of study and research, that we look forward hopefully to developments which will lend accelerated momentum to the improvement of surgery. Without research, knowledge remains static. Many branches of surgery have been static for a generation. Research dispels the tyranny of empiricism and lends a dynamic quality to an unprogressive field of knowledge. When the Forum on Fundamental Surgical Problems convenes in New York for its third meeting, it is certain that a program equally as interesting as that of the Cleveland session will await presentation.

The Board of Regents of the American College of Surgeons has appointed its committee to pass on the merits of abstracts submitted and to select the papers for presentation at the New York session of the Clinical Congress. In selecting papers for the Surgical Forum, the committee is guided by originality of thought and interest suggested in the abstract submitted by the author. The Surgical Forum is concerned more with new work than with the dissemination of old information. Each speaker will be allowed 10 minutes for his presentation.

The final selection of papers for the New York meeting (September 8 to 12, 1947) will be made by the committee in June. Anyone interested in participating in the program is invited to send during the next few months the title of his presentation accompanied by an abstract of not more than 200 words, to the Forum on Fundamental Surgical Problems, American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois.

The author may submit his paper for publication wherever he wishes. However, the editors of SURGERY, GYNECOLOGY AND OBSTETRICS will be glad to pass on the acceptability of papers presented in the Surgical Forum for publication in that journal.

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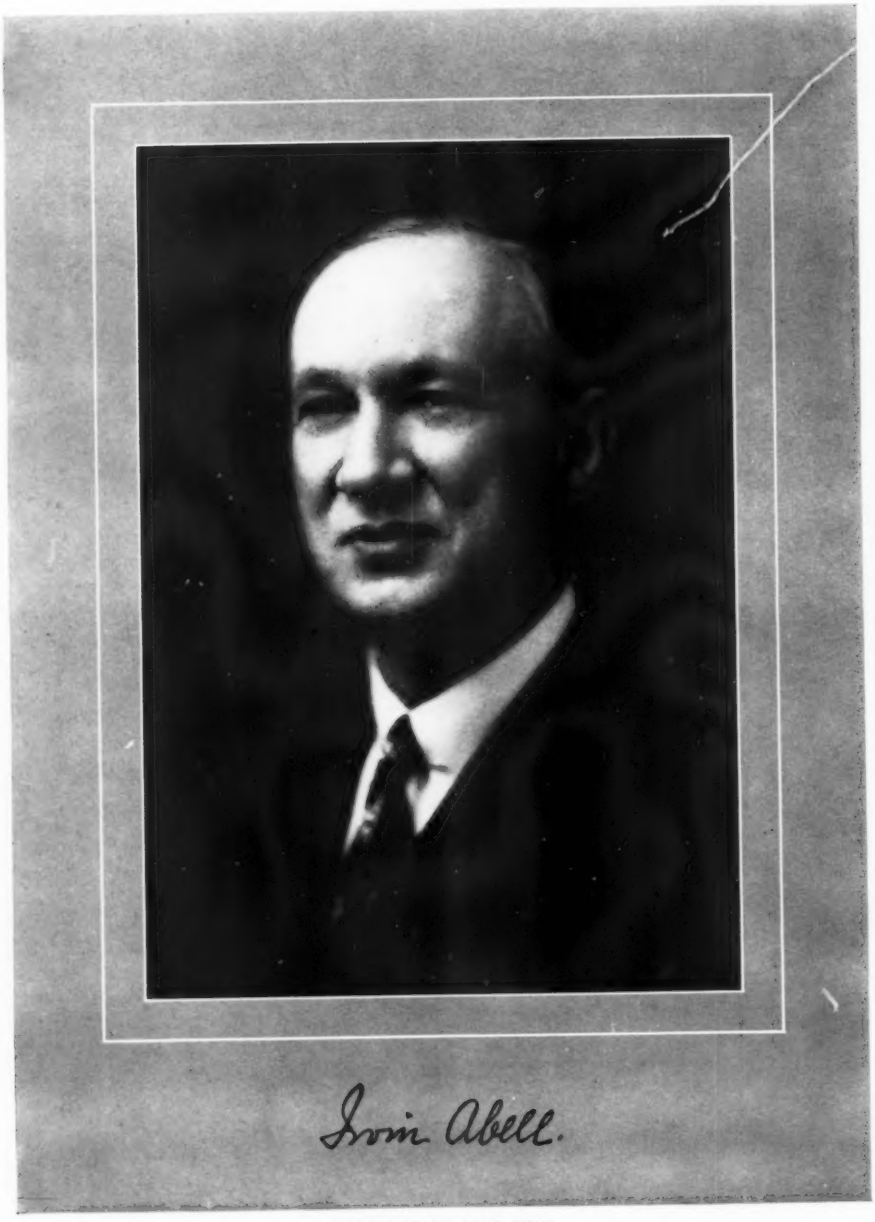

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IDEALS IN SURGERY

W. EDWARD GALLIE, M.D., F.A.C.S., Toronto, Canada

THIRTY-THREE years ago a group of very wise men founded the American College of Surgeons. It was their hope that by gathering together in such a College all the surgeons and surgical specialists who were known to be morally and ethically fit and who had demonstrated by their training and by their standing in the professional world that they were properly qualified, the standard of surgical care might be raised to the level that a great people deserves. It was hoped, too, that with the lapse of a few years the diploma of Fellowship in the College would become so desirable and so necessary that all who proposed to practice surgery would seek it and that by and by it would constitute a clear index whereby those who were qualified to do surgery could be distinguished from those who were not.

Since the day of its foundation the College has grown and prospered and it has done those things to a superlative degree for which its founders so fondly hoped.

As time went on, however, and the future of the College had been firmly established, there arose both within it and without, a demand for a definite raising of the requirements for admission to Fellowship, both in the form of longer and better practical training and of proficiency not only in surgery but also in all the basic sciences related to it. The College recognized this demand by two modifications, in the past eight years, of the length and character of the training required. Others felt, however, that all those who proposed to specialize should be forced at an early stage in their graduate training to demonstrate to a court of examiners that they were proficient in the principles of surgery and in the allied basic medical sciences. From this arose the American Board of Surgery and the boards of the various surgical specialties, to which the College elects representatives.

The aim of both the College and the Boards has been the improving of the quality of American surgery and both have been successful. The College insisted on minimum periods of apprenticeship, evidence of high moral and ethical standing, and proof that the candidate had shown ability in practice. It concerned itself with the raising of the standards of the hospitals in which its Fellows would study and work, it busied itself with advanced surgical education, as indicated by this Congress today and it is now engaged in what may prove to be its greatest effort on behalf of American surgery, the establishment of adequate graduate training. The Boards have outlined more sharply the periods of hospital training that are required and have made sure, by requiring the candidates to pass searching examinations, that they have an adequate knowledge not only of the art of surgery but of the basic sciences, without which no man can be a true surgeon.

Speaking now, not as President of the College, but as a Canadian and a most friendly

Address of the retiring President, before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–20, 1946.

onlooker, I recognize the same high motive in both the College and the Boards, and I see great virtue in what each has done. It seems to me, however, that it is a pity to have two separate roads to public recognition and that a combination of the two, with adoption of what is best in each, would add great strength to the crusade for higher standards and would ultimately serve the people best.

But while the setting up of standards for qualification to practice surgery is a step in the right direction it will prove quite futile if conditions are such that these standards cannot be achieved. What does it profit to tell a young graduate that he must serve a period of supervised training in an approved hospital, extending over a period of 3 or 4 years, if a sufficient number of such hospitals do not exist? A survey of the hospitals of Canada has shown that only a few can at present be approved for graduate training and the same lamentable state of affairs obtains in the United States as well. Only in a few of the hospitals attached to medical schools is there any attempt at the planned training of internes and residents and in very few of these, any provision for instruction in the basic sciences. How many hospitals do you know where a three year assistant residency is offered, or where regular ward rounds or conferences are held, or where supervised courses of study are provided in anatomy, applied physiology, and applied pathological chemistry? And how many hospitals do you know where internes are encouraged to make use of the libraries or to take part in surgical research? The answer is, very few. There are, of course, outstanding examples to the contrary, where the training of the interne is a major interest of the staff but when one adds up the number of these hospitals and makes up the grand total of the graduates receiving such training it will be found that the number is very small.

This is the reason for the present activity of the College in graduate training and for its effort to induce hospitals to make the necessary reorganization of their staffs and to adopt the resident system.

Unfortunately the reformation that the College has in mind is by no means so simple as one might suppose. While most hospitals are interested to a certain extent, because certification by the College that a hospital is approved for graduate training would ensure a constant supply of good internes, yet many of these hospitals balk at the radical staff reorganization involved and hesitate to put the time and effort into a teaching program that could be considered adequate. It is clear that to make a success of its graduate training plan the College will require the good will of the public and the whole medical profession and the strong support of all the Fellows.

In support of the program of graduate training I propose to discuss with you briefly the plan which has been in operation in the University of Toronto for the past 18 years. I have no thought that it is adaptable to all situations nor have I any notion that it is as good as that in many of the great American universities, particularly those with sufficient endowments to enable them to grant numerous fellowships toward graduate training. It does illustrate, however, what can be done by long term planning and by persistent effort at reform.

Twenty-five years ago the Toronto General Hospital (1,000 beds), staffed by the best surgeons in the land, all members of the Medical Faculty, had never trained a surgeon. Internes came for a year or two and departed, usually into general practice. Those who aspired to become surgeons sometimes went to New York to seek a further interneship, or more often, went to London or Edinburgh to study for the coveted diploma of Fellowship in one of the Royal Colleges. These Fellowships were won by passing the stiffest kind of examinations in anatomy, physiology, pathology and surgery and they were a guarantee that the successful candidate at at least one stage in his career had been familiar with what the textbooks said about them. They did not, however, guarantee that the Fellow had any satisfactory apprenticeship or had become a master of his craft. It was only when he returned to his home and had received a junior hospital appointment that his practical training began.

Under this system a small group of surgeons was developed from which the medical school and the hospitals selected their staffs.

Then came the era of the building of small hospitals and with it the enormous increase in the number of surgical operations. These operations, of necessity, were performed by practitioners of very little training who had learned what they knew from books, from observational tours, and from the hard experience of trial and error. I know one such hospital serving a neighborhood of six or seven thousand people where the operating rooms are busy every day from nine to one and where not a single operator ever had more than a rotating interneship. It was to try to force an elevation of the standards of education of these surgeons that the American College of Surgeons was founded.

Recognizing that the raising of standards was useless unless provision were made for training candidates to meet those standards the University of Toronto, 18 years ago, embarked on a program of graduate surgical education which gradually became standardized and which now constitutes the chief source of supply of trained surgeons for the Province of Ontario and indeed for the whole country.

The course is based on the theory that if the highest type of medical graduate is attracted to it, the best results will be obtained by combining the virtues of the apprenticeship system with those of the tutorial system. We had in mind that to ensure that the student profit most from his years of surgical residency he must be forced to undertake systematic study. To do this we arranged a definite curriculum composed both of practical training in hospital and of the instruction and study necessary to enable the candidate to face examination for the Master's degree, M.S.

The following is the minimum course:

1. A rotating interneship in an approved hospital with at least 6 months of general medicine.
2. At least 6 months in pathology.
3. One year on a general surgical ward.
4. Six months in each of three surgical specialties.

At the end of this minimum course many of the candidates qualify for the M.S. and go out to practice. Others who have shown outstanding qualities and are thought worthy of University staff appointments here or elsewhere are selected to remain as Fellows in general surgery or in one of the surgical specialties. During this period they rank as junior members of the staff and are permitted to assume independent responsibilities.

This plan of graduate training is quite elastic. As I have outlined it, it is a minimal course which may not be shortened but which may be lengthened as circumstances seem to require. Thus for the young man whose object it is to leave the university and go into practice at a distance, we suggest that he take in addition to his general surgical training, as many of the surgical specialties as possible. Six months assistant residencies in orthopedic surgery, gynecology, urology, and the surgery of childhood are of great value to him. On the other hand for the man who has made up his mind to devote himself to one of the specialties, such as orthopedic surgery, we release him from service in gynecology and urology and limit him to 6 months in neurosurgery and an extra 18 months' fellowship in orthopedics.

For men who because of their scholastic attainments, general aptitude, and qualities of mind are considered as possible candidates, at some future date, for residencies and ultimately for staff appointments, a longer course is provided. These men, after their rotating interneship, spend one or more years in the Departments of Anatomy, Physiology, Pathological Chemistry or Pathology before finally embarking on their surgical training. Then, if as assistant residents they have continued to do well, they are sent abroad for a year in some active surgical center before returning for their period of residency and ultimate appointment to a Fellowship in Surgery and a junior post on the staff. Often before finally settling down to their staff appointment these men spend a year in one of the more active producing surgical laboratories, a preparation for research work when they come home.

As already mentioned this planned apprenticeship is combined with a prescribed curriculum of studies leading to the degree of master of surgery. To win this degree the candidate must pass a stiff examination in surgical anatomy and in applied physiology and pathological chemistry. Later he faces

written and clinical examinations in pathology and surgery. Finally he must present a thesis on some clinical or experimental studies conducted by himself during his years of training.

To encourage these young men to take full advantage of their opportunities the University has given them the privileges of the anatomical laboratory and has provided first class tutors. Half of the assistant residents go to the laboratory on one night a week, and the other half on another. In this way they review the whole human anatomy in two years.

Similarly the Department of Physiology conducts a series of lectures and discussion groups on applied physiology and the Department of Pathology does likewise.

And finally, in order that these young men may be prepared for the examination for Fellowship in one of the Colleges or for certification as specialists by one of Canadian or American Boards, a series of evening discussion groups are directed by younger members of the staff on the principles of thoracic surgery, vascular surgery, neurosurgery, urology and orthopedic surgery, which many of the assistant residents may have missed in their selection of specialties.

Such a program may appear pretty extensive and to require a great deal of organization. This is not so, however, for the various departments involved have shown keen interest in graduate education and are glad to have students who are in earnest in their search for knowledge. The Department of Anatomy affords a good example. In these days when the time allotted to the teaching of anatomy to undergraduates is being so reduced that none but a superman could be expected to acquire any practical knowledge of it, the department welcomes the opportunity to teach students who have the time to devote to it and who really want to know what is under the skin.

The real difficulty in inaugurating such a planned course of graduate training will be met with in the Department of Surgery itself. The idea that as members of the surgical staffs of teaching hospitals our most important duty is to train surgeons has not been appreciated by many and is an idea which requires propaganda to inculcate. The old plan of using internes and assistant residents as servants must be abandoned if we are to get good results. Indeed, I am convinced that even in many old established teaching hospitals a rebirth in the ideals and aspirations of the staff will be required before real progress is made. I suggest to you that the ideal of the teaching surgeon should be not how skilful and impressive he can make himself by constant practice and repetition, but how many young men he can train to be as good or better than himself. Only when such an ideal is established can we hope to supply the needs of our country.

The difficulty is that busy surgeons often find it irksome to stand on the opposite side of the table assisting a young tyro in his first difficult operations. Too often they impatiently do the operation themselves or turn the job over completely and take no further responsibility for it. This, in my opinion, is poor teaching and is clear evidence that it is time for a change in the personnel of the staff. There is, of course, no excuse whatever for the old custom in which a star performer at some well known metropolitan hospital posts a list of operations for certain days in the week and does them all himself. Fortunately that sort of thing has almost passed away.

The truth is that in modern first class teaching hospitals the diagnosis should be made, the type of treatment selected and the operation performed by the resident staff under the constant guidance and supervision of their teachers. The attending staff should reserve for itself only special groups of cases on which they are conducting clinical research and those cases which obviously require more experience and skill than the assistant residents have so far acquired. These are the hospitals with huge lists of applicants and which attract the high honor graduates from near and far. Such hospitals are famous across the land for the quality of the men they produce.

But, as I have already pointed out, I feel that there should be added to this program a planned purposeful course of study, leading to an examination for a higher degree and to Fellowship in our Colleges. Such a curriculum, spread over 3 or 4 years, is no hardship to the student and I feel sure that a review of the basic sciences carried out concurrently with

clinical work, and a definite program of clinical study and instruction results in a far sounder surgical education than the haphazard methods of other days.

But even with all the teaching hospitals of America supporting such a plan, not nearly enough opportunities for graduate training will be provided. To give such opportunities to the crowds of young men now demobilized from the Armed Forces and to meet the urgent needs of the country, other means must be found to secure for these men the 3 or 4 years of clinical training necessary and to give them an opportunity to review the basic sciences. This is the basis of the present "Graduate Training" campaign of the College. It is really an effort to persuade the larger non-teaching hospitals to adopt the "resident" system and certain minimum standards considered by the College and the Boards as essential to the proper training of a surgeon or surgical specialist.

If this campaign is successful it will undoubtedly overcome the present dearth of qualified surgeons. It can be successful, however, only if it has the overwhelming support of the Fellows and it is for this that I appeal tonight.

To make it work the hospital must have a sufficient number of public ward beds to provide an adequate service for a resident staff. The attending staff must be persuaded that in return for privileges of their appointment it is their duty to train the internes. The staff should be small and should contain one or more men who have been trained in the "resident" system in a teaching hospital. They must be prepared to give much time to a teaching program, much as is done in teaching hospitals, and to compensate younger members of the staff an honorarium of some sort should be provided.

In order that an assistant residency in these hospitals may qualify a candidate for admission to examination by one of the Boards or for Fellowship in the College, provision must be made for instruction in the basic sciences. This calls for an arrangement with a neighboring medical school and may require a moderate expenditure to defray the expenses of the school. If the hospital is in the same town the problem is simple but if it is at a distance it is more difficult. It can be overcome, however, as has been done in Hamilton, Ontario, where the assistant residents come 40 miles by train to spend one evening a week in the anatomical laboratory and to attend a lecture on applied physiology.

Now while I am urging that it is the plain duty of all surgeons on the staffs of public hospitals and particularly the Fellows of this College, to join in this campaign, I should point out that the reward for hearty co-operation in it will be great and the penalty for failure will also be great. You must all have observed that with the establishment of higher standards for qualification by the Boards and the College, those hospitals known to provide approved courses of training are being so inundated with applications that they are able to fill their resident staffs with the pick of the graduating years. On the other hand those hospitals which have not been approved for graduate training or are known to provide indifferent courses, have very few applications and these only from graduates who are not acceptable elsewhere. The result is too obvious to require comment.

As the years have rolled along it has been interesting to observe the results of our planned course of training. Some of the graduates who have shown aptitude for teaching or research have won appointments on teaching hospitals and a few have become professors. The outstanding result, however, was that when the Canadian Armed Forces needed highly qualified young surgeons they were ready and were able to give our soldiers, sailors, and airmen a service that has hitherto been unsurpassed. And now with demobilization these officers are settling into civilian life and bringing to the Canadian people both in the cities and towns a quality of service of which their teachers are very proud.

This group which now has grown to seventy-five, has banded itself into a club which meets once a year to spend a day at the hospital where they were trained and to enjoy a clinical program and a dinner. To this gathering are brought all the trials and difficulties of practice and it is seldom that the trouble is so great that it cannot be solved. Through it

there has developed an excellent esprit de corps and a tradition which ensures that the general plan will long continue.

It is the opinion of this group that the young surgeon, recently certificated and accepted to Fellowship in one of the colleges should limit himself entirely to surgery or his particular specialty. At first it was thought that this could not be done and that a surgical practice could only be acquired through general work. It has been shown beyond a doubt, however, that this is wrong and that, on the contrary, it is the surest and quickest road to success. The explanation is that general practitioners are far more willing to refer surgical work to a specialist who is not in competition with them for general practice, than to another general practitioner. They do it, too, without asking a share of the fee, which is something on which to ponder.

In thinking over our experience of the past 18 years in this planned course of graduate training, I commend to your consideration the following suggestions:

First. In order that the student may acquire a satisfactory knowledge of anatomy, applied physiology, and applied physiological chemistry he should be provided with a planned curriculum of studies running concurrently with his apprenticeship.

Second. In order that he may be stimulated to engage in these studies earnestly and not perfunctorily he should be confronted with written and oral examinations.

Third. The awarding of a degree such as "Master of Surgery" to candidates who have shown a practical knowledge of the basic medical sciences and who have demonstrated to a court of examiners skill in the art and science of surgery, gives a stimulus to the whole course. Gradually the tradition develops that the M.S. is more than a diploma won by examination but that it is a written guarantee that the holder is known to his teachers to be thoroughly qualified to practice his profession. Because of this fact the attainment of the degree is much desired.

I have taken long to tell you the story of our efforts in Toronto. As I said earlier, I have no notion that our plan is an ideal one or that better plans do not exist. At this time, however, when the College is engaged in a great campaign to provide an increased supply of qualified surgeons it may be helpful to those who will be engaged in organizing and administering somewhat similar plans, to hear of the difficulties and disappointments and the triumphs of a plan that has been in operation for 18 years.

The honor of being President of this great College throughout the whole of the European and Asiatic war has been far beyond my deserts. The last Clinical Congress took place in Boston just before Pearl Harbor and you elected me to the presidency in order that you might do honor to my country which was already deeply involved in war. Thank God, as allies, we came through safely together and can now turn our minds to the urgent problems of peace. Of these none is more important than the health of the people, and, as far as this College is concerned, than that each one of our citizens, be he in the heart of the city of New York or on the fringes of Arctic civilization, may be assured, in some way or another, of competent surgical care.

INTERRUPTION OF THE DEEP VEINS OF THE LOWER EXTREMITIES IN THE PREVENTION AND TREATMENT OF THROMBOSIS AND EMBOLISM

ARTHUR W. ALLEN, M.D., F.A.C.S., Boston, Massachusetts

IT is now well established that most pulmonary emboli arise in the deep veins of the legs. Illness, parturition, trauma, and surgical procedures are conducive to thrombus formation, although this phenomenon may rarely occur in an ambulatory and otherwise apparently healthy individual. Infarct to the lung is frequently the first warning of the true situation and is often diagnosed and treated as coronary occlusion, atelectasis, pleurisy, or pneumonitis. Sudden death without warning is common and often the massive pulmonary embolus responsible is unsuspected until found at autopsy. There are some physiologic changes in the blood following trauma or illness, particularly those concerning the platelets, that must be taken into consideration regarding the cause of thrombosis. We believe, however, that stasis in the leg veins, dependent on bed rest and muscular inactivity, is in fact the chief underlying basic principle in the establishment of thrombosis.

In consideration of this problem from any point of view, one must bear in mind certain established facts. There are definitely two distinct types of thrombosis in the leg veins. Homans (11) has used the terms bland or quiet thrombosis to describe a noninflammatory process producing loose clot within the vein. Ochsner and DeBakey (16) have coined the term "phlebothrombosis" for the same condition. Both these authorities are distinguishing this type of lesion from the inflammatory thrombosis known as thrombophlebitis. The latter situation is easily diagnosed since the patient is made aware of it by pain in the leg. Associated with swelling of the extremity and fever, we have in its extreme phase "phlegmasia alba dolens" so commonly seen in the past following childbirth and often called by the layman "milk leg." This condition is not as dangerous as bland thrombosis from the standpoint of pulmonary embolism, but if allowed to run its course, causes great and often permanent disability due to persistent edema and frequent ulceration.

Phlebothrombosis is often unrecognized until serious emboli have been carried to the lung or until the character of the lesion has changed into the inflammatory process of thrombophlebitis. Bidaily inspection and palpation of the legs may result in an early diagnosis. Mild swelling of the ankle, dilatation of the superficial veins of the foot, and minor discomfort on palpation of the calf muscles are often enough to lead to the assumption that a bland thrombus exists within the deep veins of the leg. The concomitant slight elevation of temperature, pulse, and respiration is reliable evidence that phlebothrombosis is present and that a small infarct has occurred. It is in this type of thrombosis that the greatest immediate danger exists. The long, almost uninterrupted, femoral vein may contain a complete cast of loose thrombus and if this becomes detached *en masse*, the resultant occlusion of the pulmonary arteries is nearly always fatal.

The age of the patient appears to be the most important consideration regarding the frequency and seriousness of thrombosis of the leg veins. In our own cases (1) of thrombophlebitis only 5.7 per cent were in patients under 30 years of age, 12 per cent were between 30 and 40, 18.5 per cent between 40 and 50, and the peak incidence of 25.3 per cent occurred in the decade between 50 and 60. A total of 82.3 per cent were beyond the age of 40. It is apparent to us that sudden massive

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embolism is far more common in the aged. Although we have no definite evidence that phlebothrombosis is more prone to take place in the older age-group than is thrombophlebitis, there is a great deal to support this assumption in the analysis of the problem in our clinic. That some younger patients do have a bland type of thrombosis is evident, but the fulminating inflammatory thrombophlebitis is certainly more commonly seen in this age-group than in the older. We have observed all gradations of the disease. A considerable number of patients will develop an apparently noninflammatory thrombosis, especially if left untreated, and occasionally if treatment is carried out the condition will gradually change into thrombophlebitis. It is probable that this situation occurs more frequently in certain clinics and certain geographical locations than in others. Vasospasm may account for some of this variance, since in cold damp climates it may be more constant than it is in warmer and dryer regions. The chronic upper respiratory tract infections with exacerbations during the colder months may play a rôle. Certainly, our peak incidence of 32.9 per cent in the winter months as compared to 18.9 per cent in the summer seems significant.

The prevention of and the treatment of thrombosis and embolism must be considered separately. There has not been sufficient emphasis on these two distinct methods of meeting the problem. By prophylactic measures, we refer to those carried out in anticipation of thrombosis in the leg veins. Treatment of the condition in any form after the establishment of the probable or obvious diagnosis of thrombosis or infarct is a different matter. Furthermore, patients in various age-groups or according to the character of their ailment or injury may be treated differently. It is unwise to overlook these separate categories in the management of this problem as a whole. Reports on the effectiveness of one method of treatment or prevention as applied to all patients are apt to be misleading. That methods of prevention and those of treatment must overlap is obvious.

Methods of prevention of thrombosis and embolism are numerous and all should be considered on a logical basis dependent on varying circumstances. Certain primary principles such as suitable preparation of the patient for operation, gentle surgical technique, and the prevention of stasis in the leg veins during convalescence are commonly agreed upon by all clinicians. Elevation of the foot of the bed, leg exercises, early postoperative walking are all considered useful. These measures alone have apparently reduced the over-all incidence of thrombosis and fatal embolism in postoperative cases from 1 in 333 to about 1 in 800 at the Massachusetts General Hospital (20). There are many patients, however, whose type of disease, trauma, or other infirmities make it impossible to carry out such maneuvers. It seems to us that a selection of the most logical method or combination of methods must be used on individual, age or disease group indications.

Our records show that patients under the age of forty are less prone to develop the complication of phlebothrombosis and that when thrombosis of any type occurs, it is less likely to be followed by a fatal embolism. These younger individuals are basically more healthy and active, and can co-operate more readily with the clinician and nursing staff in the routine measures for the prevention of venous stasis. There are, however, many conditions afflicting this age-group that are conducive to thrombus formation in leg veins and these must be evaluated and treated accordingly. All patients in this group must be carefully watched for early signs of thrombosis. If the condition manifests itself, there is usually time to prevent a prolonged convalescence or the more important fatal embolus. Since 12 per cent of our cases of thrombosis and embolism occurred in patients between the ages of 30 and 40 years, it is probably better judgment to include this decade in the next age-group to be considered.

In patients between the ages of 40 and 65 years, we have carried out the usual general measures of prevention when possible and, in addition, have treated a small number (233) of suitable cases with dicoumarol postoperatively (2). In comparison with a control group of the same age and type, the incidence of thrombosis and embolism was reduced 75 per cent. We did not use this drug on patients

with increased prothrombin time or in those with planned multiple operations, liver or renal disease, diabetes, arthritics taking aspirin, thoracic cases, hyperthyroidism, or arteriosclerosis. Our dosage was smaller than usually recommended and was only 200 milligrams on the 2nd or 3rd postoperative day and repeated 48 hours later if the prothrombin time remained unchanged. The sensitivity to this drug in some patients, as well as the lack of measurable effect on others, was noted. No fatal bleeding took place in any patient treated. It is obvious to us that this drug is useful in many cases but that it should not be used without careful laboratory control. There are in this age-group many debilitated patients who should be considered in the next category, especially those whose disease or infirmity makes thrombosis and embolism a common occurrence and those with definite contraindications to anticoagulant drugs must be protected by other methods.

Since the danger of phlebothrombosis with death from massive pulmonary embolism increases with the patient's age, we have selected the group beyond the age of 65 for prophylactic bilateral superficial femoral vein interruption. This is done immediately distal to the profunda femoralis vein and as close to the bifurcation of the common femoral as is technically feasible. We have been so impressed by the negligible symptoms following this procedure on the normal femoral vein that we feel it should be more widely used. Up to October 1, 1946, there have been done at the Massachusetts General Hospital 458 such bilateral prophylactic femoral vein interruptions. In only one patient so treated did fatal embolism occur and in this case the vein was found at post mortem to have been divided 3 centimeters distal to the profunda. It is possible that this elderly, obese woman with a large ventral hernia had thrombosis prior to the vein interruption. It is more likely, however, that the proximal segment of femoral vein acted as a nidus for the propagation of thrombi higher in the venous system. There was a firm thrombosis in this proximal remnant of vein at autopsy. In 5 other patients who were subjected to prophylactic femoral vein division, there was a history of mild phlebitis in one or both legs following interruption. This occurred within 24 hours in 1 patient, and the longest interval was 6 weeks. In a comparable group of 458 patients who did not have prophylactic femoral vein interruption, there were 55 cases of thromboembolic syndrome with 26 instances of fatal pulmonary embolism (Table I).

The operation should be done at the time of, or within 48 hours after bed rest becomes necessary. Particular attention should be paid to this method of protection in patients with fractures near the hip joint. The danger of this complication in such cases is emphasized by Golodner and associates (10) as well as by Bauer (5). In 110 consecutive elderly patients with fractures of the hip region, prophylactic femoral vein interruptions were done in our clinic. In 2 of these thrombophlebitis did occur but none died of pulmonary embolism. In the immediately preceding 110 patients of the same type, 11 died of massive embolism. Two additional patients in this group died suddenly with signs and symptoms of pulmonary embolus but in these 2 the possibility of coronary occlusion was raised.

Almost as spectacular are the comparative studies on a group of thigh amputation cases. Veal (19) stressed the need for high femoral vein interruption in such patients for the prevention of pulmonary embolism several years ago. In 49 patients in this group receiving prophylactic femoral vein interruption, there were no deaths from embolism. In similar patients not so treated, there were 6 who were proved at autopsy to have died from this cause. In the diabetic arteriosclerotic group having femoral vein interruption, one instance of gangrene of the opposite extremity occurred. This may have been coincidental but the effect of vasospasm or even damage to the calcified arterial wall must be considered as a possibility.

We think many patients of the elderly age group can have prophylactic vein interruption prior to the main surgical procedure. It may be well to withhold it until after operations in the pelvis are completed, particularly in resections of the rectum, since venous bleeding in the field of operation is temporarily increased by division of the femoral veins.

TABLE I.—COMPARATIVE INCIDENCE OF POSTOPERATIVE THROMBOSIS AND EMBOLISM
Age group 65 years or over—October 1, 1946

Lesion	Number of cases in each group	458 cases with prophylactic femoral vein interruption		458 cases without prophylactic femoral vein interruption	
		Phlebitis	Fatal embolus	Phlebitis	Fatal embolus
Hip fracture	110	2	0	20	11*
Leg amputation	40	0	0	1	6
Gastrectomy	48	1	0	9	3
Colectomy	38	0	0	3	1
Resection of rectum	20	0	0	7	1
Cholecystectomy	23	0	0	2	0
Common duct exploration	6	0	0	0	0
Herniorrhaphy	20	0	1	3	1
Prostatectomy—benign	16	0	0	0	0
Prostatectomy—cancer	3	0	0	1	0
Radical mastectomy	13	0	0	0	1
Pelvic Surgery	12	0	0	1	0
Radical groin dissection	8	0	0	2	0
Small bowel obstruction	6	1	0	1	2
Appendectomy	5	1	0	0	0
Esophagectomy	4	0	0	0	0
Radical neck dissection	3	0	0	0	0
I. & D. Leg abscess	3	0	0	0	0
Decompensated heart disease	20	0	0	4	0
Study cases	7	0	0	0	0
Miscellaneous	38	0	0	1	0
Totals		5	1	55	26

* 4 of these were typical but not proved by post mortem.

This is not a radical method of prophylactic treatment. The operation is simple and accomplished under procaine infiltration anesthesia. Careful adherence to the operative technique outlined below will be followed by universally satisfactory results. It was not expected that such a maneuver would do more than lower the incidence of fatal embolism. It comes as an added dividend that thrombophlebitis is likewise prevented. The adequate venous return from the leg following division of the normal femoral vein and the careful avoidance of transection of lymphatics during the operation, plus the elimination of thrombophlebitis below the interruption, accounts for the almost complete absence of swelling in the leg during convalescence.

Treatment of thrombosis with or without embolism is rationally accomplished by three useful methods. These are with anticoagulant drugs, by lumbar sympathetic procaine blocks, and by deep vein interruptions. The use of heparin and dicoumarol is based primarily on the prevention of further thrombosis and thus the reduction of fatal emboli. Lumbar sympathetic procaine blocks eliminate accompanying vasospasm with reduction of swelling and pain in the legs (17). Deep vein interruptions above the thrombus preclude the possibility of fatal embolism. All of these methods reduce the period of convalescence and the late sequelae of untreated thrombophlebitis. It is evident that in some instances all of these aids to recovery may be employed on the same patient. Since it is my assignment to present the evidence for deep vein interruptions at this time, more emphasis will be given to support this form of treatment.

TABLE II.—FEMORAL VEIN INTERRUPTIONS

Massachusetts General Hospital
1937 to October 1946

	Patients
1937–1942	202
1943	165
1944	280
1945	411
1946 (Oct. .)	460
Total	1518

Homans (12) is responsible for calling our attention to interruption of the femoral veins in the groin to prevent pulmonary infarct. With a cautious approach to this method of treatment 10 years ago, we soon became convinced of certain definite facts. The operation in itself can be accomplished without harm to the patient. In no case in our institution has a patient lost his life or his limb as a result of this procedure. Most of them had no further infarct and those who did usually recovered. If the operation was done in the stage of phlebothrombosis, clots above and below the site of interruption could be removed with a carefully used glass suction tip. The amount of residual edema of the leg was dependent upon the duration of the disease. Thus in patients operated upon before thrombophlebitis began, few had any swelling of the leg during convalescence. If the operation was undertaken for thrombophlebitis, the earlier the procedure the shorter the duration of postoperative edema. This expected sequel to deep vein interruption was of surprisingly little significance as far as incapacity was concerned. There has been only one instance of postphlebitic ulceration in this group of patients.

Up to October 1, 1946, 1518 patients have been subjected to femoral vein interruption at the Massachusetts General Hospital (Table II). Four hundred fifty-eight of these have been done on elderly or debilitated patients as a prophylactic measure before, at the time of, or within 72 hours after bed rest became necessary. One thousand sixty patients were treated by femoral vein interruption after thrombosis or infarcts had occurred. Less than 5 per cent of these had further infarcts after this procedure. In most instances, these were of minor importance. In some of these, anticoagulants were used with good effect. In

TABLE III.—INCIDENCE OF THERAPEUTIC AND PROPHYLACTIC FEMORAL VEIN INTERRUPTION IN 1518 CASES

Massachusetts General Hospital
1937 to October 1946

	Therapeutic	Prophylactic		Total
1937–1942	202	0	0%	202
1943	150	15	9%	165
1944	208	72	26%	280
1945	233	178	43%	411
1946 (Oct. 1)	267	193	42%	460
Total	1060	458		1518

those with pain and swelling of the leg due to a continuation of the inflammatory process of thrombophlebitis, procaine lumbar sympathetic blocks were employed. In 5 patients in this group, death occurred following further emboli. All of these had had one or more infarcts before femoral vein interruption and thereby had a lowered pulmonary vital capacity, so that additional small emboli were sufficient to prove fatal. All but one of these 5 patients were well advanced in years and were suffering from incurable diseases. Prophylactic femoral vein interruption, if it could have been carried out, would have prevented these fatalities from embolism.

It is, of course, impossible to determine accurately the number of deaths from embolism that would have occurred in this group of 1518 patients if femoral vein interruption had not been done (Table III). In fact, a fair proportion of the operations were undertaken on the basis of shortening the period of convalescence from thrombophlebitis with its usual disabling sequelae. The majority of them, however, were in patients whose age, disease, and infirmity would have allowed us to expect that a considerable percentage of them would have had subsequent lethal emboli. This opinion is based on previous experience with this cause of death in our own hospital. Although we have not convinced all members of our staff of the rationale of prophylactic femoral vein interruption, there are few who would not urge the operation as soon as thrombosis was suspected and none would prefer other methods with the diagnosis definitely established.

The indications for this procedure now run about as follows: prophylactic interruptions 40 per cent; signs of thrombosis on examina-

tion of the legs, 35 per cent; and infarcts, 25 per cent. There was a gradual change in the trend of indications up to 1945 when a more or less constant level was reached (Table IV). Not all patients who complain of a little soreness in the calf muscles are considered to have thrombosis. Many will exhibit such manifestations after exercise, if closely questioned. Tenderness on pressure, however, should be strongly suspected. Slight swelling and dilatation of the veins of the foot are of great importance in the diagnosis. Late manifestations of the process are a positive dorsiflexion sign and definite swelling above the ankle. The concomitant slight rise in temperature, pulse, and respiration is a reliable sign of phlebothrombosis and infarct. Pain in the chest is to be considered on the basis of infarct until proved otherwise. We do not believe that phlebograms are necessary to make the diagnosis. Furthermore, the careful interruption of the normal femoral vein is definitely harmless. It is therefore obviously better judgment to err on the side of action than it is to lose a patient from a sudden massive embolism. These occur too frequently in a patient apparently doing well. Often these charts can be studied and a warning sign can be found that could have been recognized in ample time to protect the patient from that type of death. In some instances, however, there is no recorded evidence either on the chart or in the clinical notes that would lead one to suspect phlebothrombosis until proved at autopsy.

The site of *deep vein interruption* has interested us greatly. At one time, we felt that this should be determined on the basis of the level of thrombosis. We are free to admit that the best results are obtained, if the operation can be done at a level above the thrombosis. On the other hand, one must take into consideration the dangers associated with such procedures. We have had so few complications and such a high percentage of successes by selecting the femoral vein just distal to the profunda femoris as the level of division, that we now feel that this should be the site chosen in the routine case. Here, we have a segment of the deep vein that is usually free of muscular branches. This eliminates troublesome bleeding during the isolation of the vein.

TABLE IV.— INDICATIONS FOR FEMORAL VEIN INTERRUPTION—MASSACHUSETTS GENERAL HOSPITAL

1937 to October, 1946

	1937 1942	1943	1944	1945	Oct. 1946
	%	%	%	%	%
Leg signs as first symptom	59.0	56.3	41.8	33.7	37.6
Chest pain as first symptom	41.0	34.5	32.5	23.0	20.4
Prophylactic interruption	0.0	9.2	25.7	43.3	42.0

We did, in our earlier series, select the common femoral vein as the site of interruption in a considerable percentage of cases. This decision was usually based on the finding of thrombosis above the level of the superficial femoral. The occasional trapping of large quantities of blood in the leg after common femoral interruption, particularly if the femoral vein itself is not completely thrombosed, produces a dangerous immediate engorgement in the leg. This has been stressed by Dennis (7) and by Homans (13) and has been observed by us. We now feel that the added risk of exposure of the short common femoral with its multiple radicals has little advantage and is attended by sequelae unwarranting this site of interruption. If one finds the profunda femoris thrombosed at the time of superficial femoral vein interruption, it is not difficult to ligate it in continuity after the main trunk below the bifurcation has been divided. The ratio of superficial femoral vein interruption to the common femoral in our series is about 4 to 1. In the future, it will probably be in rare instances only that the higher segment of the vein is selected as the site of division. In the 5 deaths from further emboli after vein interruption, 2 occurred after the common femoral and 3 after the superficial femoral had been divided. In only 1 of these did it appear at autopsy that the profunda femoris was probably the source of the final lethal embolus.

Homans (11) believed at one time that the common iliac vein on the side affected was a logical site for interruption under certain circumstances. This attack was supported by Fine and Starr (8) and by Bancroft (4). This approach should be used only when there is obvious long-standing deep thrombosis extending well up into the iliac vein on one side.

Occasionally, in a well preserved or younger patient, it is a justifiable procedure. It has been pointed out by Homans that the collateral venous return is greater following common iliac division than it is after common femoral interruption. So frequently is it necessary to interrupt the veins on the opposite side that this difficult bilateral operation under general anesthesia seems rarely indicated. Homans (13) in a later report apparently feels that, when the thrombosis is well established in the iliac veins, low vena cava interruption is more logical, since it can be accomplished at one operation instead of two. He further points out some of the difficulties of exposure and division of the iliac vein, which can be friable and hard to manage under certain circumstances.

Ligature of the inferior vena cava has gained too much attention. Good results following this procedure have been reported by O'Neil (18), Northway and Buxton (15), Gaston and Folsom (17), and by Kern and Berman (14). Linton, in our clinic, has performed this operation in 13 patients. All have survived the procedure but 3 have developed leg ulcerations afterward. Collins and associates (6) have stressed the importance of ligation of the ovarian vessels with vena cava interruption for septic thrombosis of the pelvic veins. It is our opinion that this procedure may, at times, be life-saving. It should be reserved, however, for patients having obvious septic infarcts from thrombosis that have originated in, or extended into, the deep veins of the pelvis. Approach to the region has varied from flank to paramedian incisions. A few advocate the transperitoneal route. Linton prefers a long right paramedian incision with reflection of the peritoneum and abdominal viscera toward the left. Care must be exerted in freeing the segment for ligature, since troublesome bleeding from injury of the friable lateral veins may influence the outcome.

TECHNIQUE OF OPERATION

Technique of operation in the interruption of the deep veins of the lower extremities should be carefully considered. We may have been remiss in our earlier communications on this subject (3) in stressing the simplicity of the procedure. This was brought about by the fact that such a large percentage of our cases had been operated upon by the junior residents. We had failed to make it clear that these men had been properly instructed in the approach and the technique of the operation. Since our attention has been drawn to certain serious difficulties encountered by some surgeons who had not studied the problem beforehand, we feel that the following details are worthy of emphasis.

The patient should be placed on the table with the upper part of the body slightly elevated. Although we have had no instance of infarct during the operation, we believe that such might occur if negative pressure in the veins above the thrombosis was encouraged. The usual skin preparation for any emergency procedure is used. One per cent procaine without adrenalin is introduced by local infiltration. A vertical 8 centimeter incision is made from the crease of the groin distalward over the course of the deep vessels guided at the upper level by the pulsating femoral artery. The skin is carefully excluded by towels, which are even more important in this region than in many others. Dissection should be parallel to the course of the vessels with as little lateral division of tissues as possible. This step allows for the retraction of most of the lymphatics since transection of them, as often occurs in a transverse or an oblique incision, will increase the hazard of postoperative edema and lymph drainage from the wound. The vein is more or less mesial but often almost completely beneath the femoral artery. The artery should be freed only enough to allow gentle retraction laterally. It is better not to retract the artery with rubber tubing or ligature material, since damage to a calcareous vessel with resultant thrombosis and gangrene of the leg by this method has been brought to our attention.

The segment of vein to be interrupted lies in the exact center of the wound, if made according to these directions. The bifurcation of the common femoral vein can easily be determined by a bulge at the upper end of the superficial femoral. Exposure of the radial free upper 2 centimeters of the vein is sufficient. Ligatures for elevation of the vein are placed and not

tied at this time but the ends are held as hemostats. The anterior half of the vein is then divided transversely, halfway between the two guy ligatures. If thrombus is present at this level, it will extrude through this opening. We clear the upper segment of vein of all clot by the use of forceps and carefully apply suction through a glass tube. After free bleeding is obtained, the lower segment of vein is freed of as much thrombus as possible. Often free bleeding from the distal segment can be thus acquired. The ligatures are then tied above and below and the vein is completely divided. Transfixion ligatures are then placed on each divided end of the vein.

After irrigation of the wound with saline solution, a layer closure is accomplished with fine cotton sutures. Care should be used not to leave open an obvious divided lymph vessel. Also, the anterior crural nerve should be avoided during the closure. A complete change of gloves, instruments, and drapes is made for the opposite side. The bilateral operation should be adequately and safely accomplished within an hour. Dependent on previous inflammatory reaction in the vascular bundle and occasional friability of the vein, the operation may take a little longer. Often in a thin subject with normal structures, the operating time is reduced to 20 minutes or less to the side.

This method has been followed by very satisfactory results. Postoperative edema is minimal in most instances. If the process is subacute and thrombophlebitis with swelling in the extremity is already present, the edema lasts longer but is rarely incapacitating. There has been less than 2 per cent of wound infection in our series, and most of this has been of minor importance. Lymphorrhea has rarely occurred and is transient. Patients are treated in the same manner with or without this procedure. It has not increased the hospital stay or delayed ambulation. The only complaints have come from those occasional patients who have had trauma to the anterior crural nerve and these have not been severe.

SUMMARY AND CONCLUSIONS

1. Bilateral interruption of the deep veins of the legs is a safe and adequate method of preventing thrombosis and embolism. This procedure is particularly adaptable to aged and debilitated patients requiring prolonged bed rest and those who have had trauma to the leg or hip region. Subsequent edema in the legs, following division of the normal superficial femoral vein, is negligible.

2. Treatment of phlebothrombosis by thrombectomy and interruption of the deep veins of the legs is highly satisfactory. Early diagnosis permits the division of the vein above the thrombosis at the superficial femoral site. It is rarely justifiable to perform a higher division of the venous system under any circumstances.

3. Thrombectomy and superficial femoral vein interruption is an effective method of treatment in early thrombophlebitis. Patients with continued infarcts following this procedure should have anticoagulent therapy. Those with continued pain and swelling of the extremity following femoral vein interruption should be treated by lumbar sympathetic procaine blocks.

4. Division of the common femoral vein is not recommended. If the profunda femoris is thrombosed at the time of superficial vein interruption, this radial can be separately tied in continuity.

5. Bilateral femoral vein interruptions should be done since often the fatal embolus arises in the opposite, apparently normal, vein.

6. The collateral venous circulation is better following common iliac interruption than it is after common femoral division. Occasionally, in a definitely unilateral process extending into the pelvis in a good risk patient, the common iliac vein may be the site of choice for operation.

7. Inferior vena cava ligation should be reserved for those patients who are having repeated septic infarcts. These emboli may have originated in the pelvic veins or progressed to this area by direct extension from the leg veins. In pelvic suppurative thrombophlebitis, the ovarian or spermatic vessels should be interrupted at the time of vena cava ligation.

8. There have been no deaths and no patient has lost a limb as a result of femoral vein

interruption in 1518 patients so treated in the Massachusetts General Hospital.

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Franklin H. Martin, Colonel, M.C., U.S.A., member Advisory Commission, Council of National Defense, World War I.

THE AMERICAN SURGEON, A. U. S.

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IN choosing the accomplishments of the surgeon of World War II as the subject of this first Franklin H. Martin Lecture, I realize that I have set myself a difficult task. The American Surgeon, A.U.S., is a Rip Van Winkle, already packed off into the Catskills for a long sleep. His return to the platform may be accepted with tolerant politeness, but his experience is considered an affair of the past without reference to the immediate future. An acceptance of the challenge to present this subject means that I hold a deep conviction that there are many significant things that have not yet been said about the surgical experience of the recent war.

The full impact of war experience on surgical theory and concept has by no means been measured. One reason, perhaps, is the preoccupation with novelties that characterizes the profession of today. No novelties emerged from the past war. There is no fancy packaging that leads the buyer to believe he can obtain something new and important. There were few, if any, novel technical achievements. In fact, war tends to submerge the importance of technical details. Surgeons from all sections of the country are brought together in a common task with the result that specific techniques, oftentimes taught as essentials in a parent school, are recognized as unimportant details when placed against a broad perspective. The vast experience of war provides a view of surgery comparable to an aerial reconnaissance photograph in which the significance of a single bomb crater is lost in the display of the pattern as a whole.

At the risk of repeating what may be familiar material, I shall point out certain aspects of surgery that have profited by the clarification that can come only from the impact of broad experience.

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SHOCK

The nature of the shock exhibited by a wounded man has been made a matter of mystery for many years. During World War I, observations on the shock of wounded soldiers showed that "the vasomotor center was efficiently at work and the heart was capable of assuming any reasonable burden placed upon it" (4). Attention then centered on the discrepancy between blood volume and the capacity of the vascular bed. A fruitless search for the "lost blood" led to the concept that the fluid portion (plasma) had been lost through the capillary wall by a generalized increase in its permeability. An assumption was made that toxic products derived from injured tissue damaged capillaries remote from the site of injury.

In the period between the wars, this loss of plasma was localized more definitely to the areas that had been injured, and both the assumptions of a traumatic toxemia and of a generalized change in capillary wall permeability were questioned. Observations were extended beyond the intravascular space to the interstitial fluid compartment. Certain electrolytes, sodium and chloride, were found to move freely in the vascular and interstitial spaces but observed to meet an effective barrier to entering the cell; others, notably potassium, magnesium, and phosphorus, were admitted to cells, even though in low concentration.

The toxicity of potassium when given intravenously and the high level of potassium observed in certain instances of advanced shock led to the concept that it might represent a noxious agent. It was even referred to as a possible "H-substance" (19), a generic term that had been used to designate the products of tissue injury. At any rate, no one considered that an actual deficit of potassium or other electrolytes within the cell might be an important component of injury.

World War II was started with the concept that plasma for the intravascular space and

sodium chloride solution for the interstitial space were therapeutic measures adequate to re-establish equilibrium in a wounded man. Experience in North Africa immediately demonstrated the inadequacy of this therapy and showed the necessity for whole blood (15). As soon as equipment could be obtained a blood bank, organized by the Theater with service troops as donors, supplied the full needs of the Mediterranean forces to the end of the war.

The loss of whole blood following wounding far surpassed that estimated at the beginning of the war, and the degree of shock closely paralleled the amount of blood lost (16). The obvious explanation of why whole blood is needed rather than plasma is that replenishment of red cells maintains the required oxygen-carrying capacity. Future investigation will test the validity of certain less obvious explanations. Red cells form an appreciable portion of the *mass* of blood and a portion that cannot be lost into an area of trauma without actual disruption of vessel walls. The physical action of cells as a filler for the intravascular space may be significant, because it is not clear how long plasma administered in the face of a low hematocrit remains in circulation.

Again, there is the problem of the electrolytes to which I have referred. Potassium appears in considerable concentration in the urine following hemorrhage (18). From what cells it is lost and by what mechanism is not clear. The specific effects of the departure of the potassium ion from cells on recovery from shock or recovery from other effects of the wound remain to be explored. Suffice it to say that potassium and also phosphorus are virtually lacking in plasma but present in large quantity in red cells.

Other considerations have led the attention of the surgeon beyond the capillary wall, across the interstitial compartment to the cell. The term *irreversible*, borrowed from elementary chemistry, is found in writings on shock. The issue is kept clear only if its use is restricted to the effects of shock and not extended to the condition of shock itself. Shock, defined as reduced blood volume flow, is reversed by replacement of blood volume. Selective death of organs or tissues brought about in whole or in part by shock is not reversible. It is probable that each tissue and organ has a different threshold at which it succumbs to asphyxia. Functional impairment or complete suppression of function may appear in certain organs, for example the kidneys, and delayed death of the entire organism ensue, despite the fact that other organs have been "resuscitated" and the direct effects of the missile repaired. In this sense the effects of the wounding as reflected on the kidney in many cases have been irreversible—at least with our presently available modes of therapy.

In the past war replacement of lost blood reached an extraordinarily high level of effectiveness. It is certain that hundreds of injured men survived the immediate effects of wounds that under slightly less favorable circumstances would have proved fatal. Irreversible shock as such was not encountered. An appreciable number of the wounded survived, however, only to die about the tenth day with complete anuria. A chain is as strong as its weakest link. When links are strengthened where the chain has broken previously, new weak spots appear simply because the chain holds to test them. The obvious weak link in the severely wounded in this war was the kidney.

Death from suppression of urine attracted attention for two obvious reasons. First, the syndrome is readily recognized provided the urinary output is observed; second, the time of death is quite remote from the immediate sequelae of the wounding. When the chain breaks within the first 48 hours of wounding it is oftentimes impossible to tell which of many links gave way first. Thus it is entirely possible, indeed there is evidence to indicate, that other organs may be mortally damaged by the indirect effects of trauma. The liver and the adrenal cortex come to mind as organs that deserve careful study in this respect. Any specific effects of the functional suppression of these organs are so likely to be obscured by the whirlwind of events in the first 48 hours after severe wounding that clinical observations still remain inexact and fragmentary.

At one time in World War II there was a trend which, if allowed to develop, might well have separated the treatment of shock from surgery. The following is an extract from an

official report of the Surgical Consultant, North African Theater of Operations, dated 2 July 1943:

"Hospitals receiving battle casualties from the field establish a Resuscitation Ward to which patients requiring resuscitation are sent from the Reception Ward. A 'Resuscitation Team' of Medical Officers is constantly on duty. This is an efficient arrangement and absolutely essential when casualties arrive in overwhelming numbers. There is one drawback which, if clearly recognized, may be guarded against. Resuscitation comes to be regarded as a subspecialty of military surgery and as such becomes a goal in itself. One central fact must be kept in mind and, although it appears obvious, it is often overlooked both in theory and practice. *A wounded man is resuscitated not only to save life but to prepare him for necessary surgery.* Starting from this axiom a number of principles become clear.

"(1) Any delay in resuscitation prolongs the crucial interval between time of injury and operative treatment. Also, delay in the reversal of shock increases the deleterious effects of circulatory failure. Delays in resuscitation procedures have been observed that were attributable to:

"(a) Insufficient grasp of these fundamental principles, chiefly on the part of junior grade ward officers with inadequate training in surgery. This is of course a reflection on:

"(b) Failure of the operating surgeons to follow closely the clinical course of patients in the Resuscitation Ward. They wait for them to be 'served up' to them. This divorce of surgeon from shock is a disquieting outgrowth of the war that cannot be too strongly condemned. Resuscitation in every case being prepared for operation is an integral part of the surgical management of trauma and must remain so if optimal results are to be achieved."

In the Italian Campaign, Dr. Henry K. Beecher made many important observations, both clinical and quantitative, on the preparation of the wounded for surgery and presented a broad definition of resuscitation that includes operation as an essential component.

"The enemy has produced the worst wound he could, and its consequences are cumulative—dehydration increased by unusual fluid loss in sweat and vomitus, continuing hemorrhage or plasma loss, pain making rest impossible, increasing emotional exhaustion, developing infection—these and other factors are set in operation by the initial wound. Their progress in the seriously wounded is to be checked in most cases only by surgery or by death. Resuscitative measures give a temporary stay and make successful surgery possible in the severely wounded; but in most cases true release from the consequences of the wound is effected only by surgery. Surgery is not only the goal but is itself a part of resuscitation in the broad sense. Any other view is likely to lead to unfortunate separation between the activities of the 'shock team' and those of the surgical team. Care of the wounded man must be continuous and supervision uninterrupted" (2).

This point of view, developed during the war, has a direct bearing on such practical matters as the design and placement of surgical hospitals. Converging litter carries and ambulance shuttles come to a junction at the Clearing Station of the Division. Here casualties are sorted and their disposition determined. During the campaign in Sicily (6) it was determined that the surgical hospital for treatment of the severely wounded should be placed alongside of the Clearing Station so that a short litter carry would place the casualty in the hands of a competent surgical team equipped not only for resuscitation in the narrow sense but for the major procedures of surgery. One reason for this location of the hospital was to avoid the holding of a seriously wounded patient in a station not equipped for surgery while futile efforts were made by the infusion of plasma or blood to prepare him for another ambulance lift, even though it were a short one.

Upon entering the surgical hospital the wounded man's response to blood replacement therapy was carefully observed. If the response was transient or unsatisfactory, particularly in the case of an abdominal wound, it was assumed that either continuing hemorrhage or spreading infection was present and operation was immediately undertaken. By this aggressive course many lives were saved.

To clarify thinking, resuscitative measures carried out in the field, forward of a surgical hospital, were considered as temporary and designed only to preserve life during transportation. They thus became both qualitatively and quantitatively different from those combined with surgery. It was necessary to rely on plasma as the chief measure to support the patient during transport, but this was used in minimal amounts without intent to restore the volume flow to a normal level. Resuscitation within the hospital included additional plasma, whole blood, initial wound surgery

and ancillary measures such as bronchoscopy, oxygen therapy, and nerve block to relieve pain.

The resuscitation of severely wounded soldiers provides a lesson pertinent to the management of the victims of civilian accidents. In transportation to a hospital equipped for major surgery, only such delay should be countenanced as is essential to deliver the patient to the hospital alive. Similarly, hospitals likely to receive such patients must be organized so that there can be no delay in the institution of the resuscitative measures that must carry the patient to the operating room and through the essential life-saving surgical procedures.

What has been called "the pathology of shock," (Moon) that is, the microscopic changes in the tissues that are attributable to shock, has long been a matter of discussion and confusion. Blalock succinctly stated: "The length of time that the patient lives with an inadequate supply of blood and oxygen to the tissues determines the alterations that are to be found in them" (3). Again, Yandell Henderson remarked that "unless one is burned alive, the tissues of one's body always die of asphyxia" (10). It is apparent that postmortem studies must distinguish between those changes that are common to death from whatever cause, and those changes that result from the exposure of the tissues to the insult of a period of reduced blood volume flow. Such a beginning has been made on the basis of war material by Dr. Tracy Mallory (13), and it may be expected that another area of confusion in the so-called shock problem will be resolved, at least in part, by the establishment of the pathology of shock as contrasted with the morbid anatomy of death.

WOUND INFECTION

The subject of wound infection is so closely linked with the surgical management of wounds that it will be dealt with briefly. Only rarely does anaerobic infection complicate the injuries of civil life, yet it may reach almost epidemic proportions in war. The predominance of bullet wounds over high-explosive shell wounds until the year 1914 tended to keep the incidence of gas gangrene low; then came the catastrophic experience of the British Expeditionary Force in France and Flanders. The striking reduction in the incidence of gas gangrene in the latter periods of World War I proved, as Archibald states: "The incidence of gas gangrene can be taken as the one reliable yardstick by which to measure improvements in field evacuation and in forward surgery"(1).

Taking up the subject during the campaign in the Western Desert, Major J. D. MacLennan (12) of the Royal Army Medical Corps clarified the approach to anaerobic infections for the surgeons of World War II. He attacked the "widespread impression that the anaerobes constitute a small and highly dangerous group of organisms rarely found, difficult to grow, and productive only of spores, bad smells, tetanus, and gas gangrene." He showed, further, that the absence of anaerobic bacteria from war wounds is a "matter for surprise rather than satisfaction, their presence for resignation rather than alarm." MacLennan's emphasis on the fact that anaerobic infections are clinical, not bacteriologic, entities provided the substance for a vigorous educational campaign. Setting up the entity of *anaerobic cellulitis* as distinguished from *clostridial myositis* brought clarity of definition and an understanding of anaerobic infection to hundreds of surgeons upon whom rested the responsibilities for preservation of life and limbs. That this concept needs emphasis in civilian teaching and the civilian practice of the surgery of trauma is immediately apparent to surgeons returned from the war.

It is difficult now to recapture the confusion in the prevailing doctrines regarding sulfonamide prophylaxis and therapy that was carried over from civilian surgery to military surgery at the time of Pearl Harbor. War experience completely unseated the dangerous teaching that wounds could be "salted down" with "sulfa drugs" as an alternative to prompt surgical treatment. The civilian surgeon entered World War II obsessed with the efficacy of the topical application of the sulfonamides in the prophylaxis of wound infection. He returned from war with faith in the therapeutic use of penicillin and, at times, sulfadiazine, admin-

istered systemically to control impending or established invasive infection.[1]

The ability to check invasive infection by chemotherapy freed the surgeon from inhibitions that long have stayed his hand. The fear of fanning the fires of infection by the surgical manipulation of infected tissues following trauma was banished. A bold revolution in the management of wounds took place. This has led to changes in the basic concept of the surgical approach to wounds and traumatic injuries.

REPARATIVE SURGERY

By the acceptance of the term "reparative surgery" in a War Department Technical Bulletin (TB MED 147, March, 1945), the Surgical Consultants' Division of the Office of The Surgeon General gave official recognition to a concept of wound management that originated in the Mediterranean Theater of Operations. The validity of the concept was strengthened by subsequent experience in the field. The cessation of combat in northern Italy found it firmly established among the surgeons of the Theater.

This phase of wound surgery follows the "débridement" or initial wound surgery established as a basic procedure in World War I and perpetuated in the recent war as the keystone of wound management. Reparative surgery has been described as follows: "A highly significant and far-reaching advance in military surgery has taken place in the base hospitals with the development of what may be called reparative surgery. Wounds left unsutured at the initial operation are routinely closed by suture, usually at the time of the first dressing. With the use of penicillin as a safeguard against infection, the management of wounds complicated by fracture or joint involvement has been revolutionized. Surgical procedures in special fields of surgery—thoracic, craniocerebral, abdominal—have also been radically altered by the application of similar principles. The significance of this development and its effect on returning an increased number of wounded soldiers to duty and in preventing deformity, disability, and death in the seriously wounded can hardly be overestimated.

"Reparative surgery is not to be confused with the reconstructive surgery of the Zone of the Interior. Reparative surgery is designed to prevent or cut short wound infection either before it is established or at the period of its inception. Once established, wound infection is destructive of tissue and at times of life. In many instances it permanently precludes the restoration of function by the most skillful reconstructive efforts.

"If the initial wound operation has been a complete one, wounds of the soft parts may be closed by suture on or after the fourth day. The dressing applied in the evacuation hospital is removed under aseptic precautions in an operating room of a general hospital at the base. Following closure, the part is immobilized preferably by a light plaster encasement, or if this is impractical, by bed rest" (5).

A parallel evolution in wound management, differing only in unimportant details, took place in the Central Mediterranean Forces of our allies, with whom a close and cordial professional relationship was enjoyed from the time of the invasion of North Africa. Brigadier Harold C. Edwards (9), Consulting Surgeon, A.F.H.Q., in a Report to the Director of Medical Services covering the period March 1 to October 31, 1944, referred to the subject as follows: "It is not too much to claim that the surgery of war wounds has undergone a radical change since the first mass experiment in delayed suture was planned before the battle of Cassino . . . .

"*The accepted treatment of all wounds . . . . is a two stage operation*[2] irrespective of whether an open fracture exists or not. This conception has led to an immense diminution in invalidism as a result of chronic sepsis, of pain and discomfort, and of numbers of dressings. It has led to an incalculable saving of hospital beds (one analysis has showed the saving to be

[1] That deep instinct of the surgeon to annoint the wound with healing balms, salves or antiseptics and to keep it open with setons, tents or tubes, finds its roots in the mysticism and polypharmacy of the ancients. It still plagues our craft in the usage of the precise tools of chemotherapy and antibiotic agents. A long line of illustrious surgeons, basing their experience more often than not on the battlefield, have combatted the doctrine that the healing of a wound is governed by the topical applications of the surgeon. This line of dissenters extends from Lord Moynihan, the great sceptic of world War I, through Lister, Wurtz, Paré, Henry of Mondeville, Hugh of Lucca and Theodoric, Celsus, and the Good Samaritan, to Hippocrates.

[2] Italics by the writer.

as 24–35) and, in consequence, of manpower. Men are fighting now[1] who have already twice recovered from wounds since the 'D' Day for Cassino—May 12th. Furthermore, the resulting scars have been firmer, less adherent, and less liable to break down."

In the Royal Army Medical Corps the terms "delayed suture" and "secondary suture" were retained, and the program as a whole referred to as the treatment of a wound by a two-stage operation.

The adjective *reparative* was chosen by the U. S. Army Medical Corps to set apart the phase of surgery under discussion from the initial operation (débridement) that precedes it and the reconstructive surgery that may follow. Reparative surgery has been referred to as "surgery of necessity" for a limited time exists following the initial surgery during which its maximum benefits may be secured. It is neither emergency surgery on the one hand, nor elective surgery, in the sense that it may be postponed, on the other. The word "reparative" was chosen with reference to the technical procedures that repair damaged and distorted anatomic parts; also, it indicates that the surgery coincides with the period of greatest biologic activity in wound repair. This starts on the fourth day, the time selected on purely clinical grounds as the optimal time for surgical repair of a soft tissue wound. There is no sharp end point, but for the simple wound the optimal phase for surgery closes at approximately the tenth day. This time interval for reparative surgery is fixed by biologic laws to which military planning must accede, unless grim necessity demands sacrifice of that part of the potential combat strength of the force evacuated as "lightly wounded."

The application of the procedures of reparative surgery requires an analysis of a wound in terms of the structures that have been damaged, for the repair of each tissue and structure is subject to different laws. It also stimulates a precise analysis and recast of terminology to achieve uniformity in definition and clarity in thinking.

It is important that the scope of the term "reparative surgery" be clearly understood. It is by no means synonymous with "delayed primary suture," "delayed suture," and "secondary suture." Reparative surgery defines a phase of wound management during which these procedures, referred to as the second stage of the two-stage operation by Edwards, are carried out. In addition, other operations such as decortication of the lung, the early removal of foreign bodies, the repair of nerve injuries, and the final reduction of battle fractures are considered as reparative surgery because they are "designed to prevent or cut short wound infection either before it is established or at the period of its inception" or concerned with restoration of the function of the part by anatomic repair.

Wounds are referred to as "simple"[2] or "soft tissue" wounds when the injury is confined to skin, subcutaneous tissue and fascia, and muscle damage is not extensive. A "complex"[3] wound has, in addition to the soft tissue wound, damage to nerve, bone, tendon, joint or major vascular trunk, or extensive damage to muscle that will materially interfere with function. In the management of a complex wound subsequent to the initial surgical débridement, separate consideration must be accorded each component part of the wound, such as the wound of the soft tissues, the wound of the bone, or that of the nerve. The timing, the sequence and the extent of the reparative surgical procedures carried out on a complex wound are determined by its component parts, their extent and nature, and the wide variety of combinations in which they may be present.

Thus, the term "reparative surgery" designates a phase of wound surgery applicable to complex wounds as well as simple wounds,

[1]The report is dated 6 December 1944.

[2]The term "simple gunshot wound" was defined and used by G. J. Guthrie in recording the opinions and practice of the Surgical Department of the British Army at the termination of the Wars in Spain, Portugal, France, and the Netherlands, in 1814 and 1815. Simple wounds were "Wounds in Parts of no vital Importance or Comparative Consequence in the Human Frame."

[3]Various terms have been used to describe wounds that are more extensive than simple wounds. The adjective "compound," is closely linked by usage with open injuries of bone and joint and has thereby acquired a specialized significance. The term "complicated" implies "complications" such as secondary hemorrhage or infection and for this reason is best reserved for wounds with a sequential pathologic entity. Also, a specialized meaning has developed in bone and joint surgery, and a "complicated" fracture is one with adjacent injury to other structures such as a nerve or joint. In the sense used here, a *complex wound* is one with multiple and important anatomic components that are interrelated. It contrasts neatly with the simple wound of the military surgeon of the past.

rather than any single technical procedure such as delayed suture of the soft tissues. It includes a wide variety of operative procedures for complex wounds, as well as closure of the skin and underlying soft tissue. Also, as a comprehensive term, it includes a number of methods of closure of simple wounds that find a constant application when large numbers of casualties are being treated. The terms "delayed primary suture" and "secondary suture" describe the closure of the skin in terms of the time interval that has elapsed before closure is attempted. Universal agreement is lacking as to the actual time intervals that are implied by the use of these two terms, and experience has shown that, after all, no sharp line exists so far as the ultimate result is concerned, provided the surgical technique employed is adapted to the specific problem at hand. For this reason the inclusive term "reparative suture" has come into use, implying a delay and contrasting with primary suture.

In general, the following principles will be found valid in the management of a simple wound or the soft tissue component of a complex wound.

1. When the initial surgery (débridement) has been complete and the wound has been protected from subsequent contamination by an occlusive dressing and adequate splinting, the optimal time for closure is the fourth postoperative day. At this time muscles and fascial planes may be sutured with catgut, cotton or silk, and closure of the skin defect may be aided by the advancement or rotation of flaps, or the application of a split thickness graft.

2. As the time interval is increased beyond the fourth day, the feasibility of anatomic layer closure diminishes and there is a steadily increasing number of cases in which closure must be performed by single sutures passing through all layers.

3. On or about the tenth day it will be found necessary to undercut the cutaneous margins, with or without the removal of surface granulation tissue, to obtain skin approximation. The incidence of kindly healing will be appreciably lessened and the ultimate scar will tend to spread.

4. Again, as the time interval is extended beyond the fourth day, there will be found an increasing indication completely to excise the wound before suture, thus to restore flexibility and permit layer closure. This procedure is limited to wounds in anatomic regions where additional loss of tissue will not interfere with the ultimate functional or esthetic result. In very late wounds (3 weeks to 6 months) complete wound excision is an essential prelude to closure by suture, and may be necessary or advisable preceding skin grafting.

5. When the initial surgery (débridement) has not been complete and devitalized tissue remains in the wound, a purulent exudate, at times associated with a foul odor, will be apparent by the fourth day. Under these circumstances, the residual necrotic tissue may be excised and the wound closed immediately; or, following excision, the wound again may be left open and closure undertaken when it is certain that all dead tissue has been removed and invasive infection is not to be reckoned with.

6. When invasive infection is present, free drainage is established and tissue devitalized by the infection or by the original trauma is excised. The interval before closure may be attempted varies with the severity and extent of the infection, but usually falls within the 10 day period following the operation.

Management of the soft tissue component of a complex wound is modified by the treatment that must be directed to those injured structures that are important to the ultimate function of the part. In a complex wound the goal of reparative surgery is not limited to the closure of the soft tissues and skin but extends to the repair of the wound of the bone, the nerve, or the important muscles that have been divided. In general, early closure of the skin is greatly desired to exclude further bacterial contamination, but it may be delayed deliberately. For example, following reparative suture of a transversely divided quadriceps femoris or deltoid muscle, the skin may be left unsutured in selected cases to provide free escape for blood and wound exudate. Skin closure is then carried out in approximately 4 days. Battle fractures are complex wounds and usually the most important component of the wound is the fracture rather than the soft tissue defect. After accurate re-

duction is secured, closure of the muscles over the fracture site is the most vital step of reparative surgery. Suture of the skin may be delayed, or if the defect is small, spontaneous healing may be anticipated long before the fracture is united. Again, complete or partial division of a nerve may be the most important component of a wound. Here the first step may be complete suture of the soft tissues and skin to obtain clean healing with minimal scar formation. Repair of the nerve then may be undertaken at a 3 week interval. When nerve and bone are both injured, still more elaborately staged procedures may be indicated, always with the goal of the restoration of the ultimate function of the extremity in mind.

The surgical principle that has emerged may be summarized as follows: Following an open traumatic injury, excision of dead and devitalized tissues should be done at the earliest opportunity. This may be considered as an initial operation and care is taken to conserve all viable parts that are important to subsequent function. Dressings and splinting are designed to minimize swelling and prevent further damage to structures by motion. Invasive infection is held in check by systemic chemotherapy. The patient may then be transported to receive the full benefit of whatever specialized technical skills are required for the reparative surgery of complex injuries. The application of this principle in civilian trauma is readily apparent.

THE PATTERN OF TRAUMA

The war experience with traumatic injury emphasizes the need for further understanding of what may be called the pattern of trauma. When individuals are simultaneously subjected to trauma or sequentially exposed to the same trauma, the resulting injuries conform to a type pattern. This has long been recognized in civilian injuries, and entities such as "miner's elbow" and "bumper fracture" are surgical classics. It is a familiar finding in disasters and I need only mention the Cleveland Clinic fire and the Boston Cocoanut Grove fire to emphasize the necessity for immediate recognition of the pattern of trauma. There were similar incidents during the war, such as the Bari air raid and, of course, most notably the atomic bomb attacks on Hiroshima and Nagasaki. Recognition of the pattern of trauma must be prompt in disaster to point the way toward effective treatment of the survivors. A recurring pattern in injuries sustained sequentially under similar circumstances leads the surgeon to propose preventive measures.

PREVENTIVE SURGERY

World War II witnessed a rudimentary but clear appreciation of preventive surgery, an undeveloped phase of our craft. Preliminary explorations were made in the use of protective armor against flying missiles. Protective body armor in the form of a "flak suit" was adopted early by the Air Force. Careful analyses on the lethality of weapons and the distribution of wounds document the assertion by DeBakey (8) that the application of existing knowledge on body armor might "reasonably be expected to reduce the number of those killed in action by 12 per cent and of those wounded in action by 8 per cent." Although the war ended before body armor could be used in any area of land combat, other protective devices, in addition to the familiar steel helmet, were introduced by surgeons. Sir Alexander Hood (11) points out that the familiar crash helmet of the British Army was designed by a neurosurgeon (Hugh Cairns). Surgeons of the European Theater of Operations (7) assisted the medical service of the Air Force in a vigorous effort to prevent high altitude frostbite. With protective equipment and procedures this crippling injury of expert bomber crews was virtually eliminated. Ophthalmologists conducted extensive field studies on the use of shields designed to protect the eyes from the hazards of land mine and booby trap explosions.

The control and prevention of blast injuries of the ears were effected by joint study of Ordnance and the National Research Council. The incidence of aero-otitis, a common disability that grounded highly trained air crews was greatly reduced by control measures. Footgear effective in the prevention of trench foot was developed through Medical Department liaison with the Quartermaster. Tetanus, an ancient scourge of the battlefield, was vir-

Members of the Council of National Defense and the Advisory Commission Seated, left to right: David F. Houston, Josephus Daniels, Newton D. Baker, Chairman of the Council; Franklin K. Lane, William B. Wilson. Standing, left to right: Grosvenor B. Clarkson (Secretary), Julius Rosenwald, Bernard M. Baruch, Daniel Willard, Dr. Franklin H. Martin, Hollis Godfrey, Howard E. Coffin, Walter S. Gifford (Director).

tually eliminated by the inoculation with toxoid.

It is clear that this preventive phase of surgery must be developed with vigor and imagination to keep apace with the traumatic hazards of modern life, or surgery will remain solely a salvage service. Although the surgeon is historically the senior practitioner of the battlefield, his place of importance has been yielded to the expert in preventive medicine in the conflict of mass armies. With the awful increase in the lethality of weapons and the destruction of the civilian population as the strategic objective of the enemy, it seems unlikely that military surgery will ever regain its ancient position by virtue of its salvage function alone. As the military power of this country depends upon highly specialized personnel operating extremely complicated weapons and machines, the military surgeon of the future must be an expert in the prevention of traumatic injury in addition to its alleviation.

THE DOCTOR AT WAR

Having discussed certain ways in which his war experience may have modified surgical theory and concept, I shall deal briefly with broader phases of the experience of the American Surgeon, A.U.S. Pearl Harbor found the civilian medical profession in a maze of poorly integrated but highly developed specialism in remedial medicine. The prevailing tactical

situations of World War II permitted the useful application of a wide variety of specialized techniques to injury and disease. The range of these techniques had not been anticipated in the plans of the Army Medical Department, and particularly during the early phases of the war, Medical Officers found difficulty or frustration in their attempts to apply their full potential. An unenlightened attitude of Command toward the mission and operation of the Medical Department was not wholly surprising. It cannot be assumed that tough-bodied and tough-minded laymen will have a full appreciation of the functions of doctors and hospitals. Even a lay Board of Trustees in a civilian hospital requires education. Medical staff officers only rarely were vested with the authority that is derived from having the ear of Command. It was difficult for them to make the voice of Medicine heard above the clamor. The wound surgeon, by virtue of his direct and clearly understood mission, fared better than his colleagues in internal medicine and neuropsychiatry. Preventive medicine, in so far as it pertained to sanitation and hygiene, was well carried out; but warnings and advice regarding hazards that had not been visualized in Army peacetime training and discipline were likely to pass unheeded. These hazards were often the unforeseen results of the use of the tools of war (airplanes, tanks), or exposure to rigorous climatic conditions (trench foot, frostbite), or the contact of troops with diseased populations (malaria, venereal disease). Underlying these physical hazards was the all-pervading danger that came from the nature of war itself. In the lay terms of Eric Sevareid, "Modern war has become altogether too much for the delicate anatomy of the human brain and nerve cells. A sight, a sound, a hot breath of blast can turn men's minds to water . . . ." It was difficult to reach the Command with authoritative advice regarding these hazards and it was not always followed when received. A total health program that utilized the knowledge and experience of the medical profession regarding "man and all that concerns him" (11) was never envisioned.

There is nothing to be gained by destructive criticism at this late date. There is, however, a lesson to be learned by a recognition of the forces at play. The rôle of the doctor in war always must be that of his rôle in civilian life—an advisor. There are only two essentials: first, his advice must be sound and, second, it must be heard. The decision as to whether it is heeded will, as in the case of the individual patient, rest with the Command. A statement made recently in a subdivision of the War Department shows how vigorously Command preserves its right to disregard expert professional advice.

With respect to the function of the Surgeon General, a policy was proposed "whereby the technical services will exist solely to serve the needs of combatant forces without the power or authority to dictate policy or to influence operations by imposing the will of the technical representatives upon the will of the combat Commander." No one can take issue with the validity of this principle in time of national danger. The profession harbors no ambition to "impose its will" on a Commander or to "influence operations" that, in his judgment, are essential to the common defense. Disease, not the Doctor, imposes its will on the Commander; man's physiologic capacities limit and influence operations. These are the decimating forces that can dictate policy to the Commander. It is both the concern and the responsibility of the Army Medical Department that this shall not happen.

The Command must recognize that the country in peace and war alike demands high standards in the care of the injured and sick, and that the individual Commander is not free to exercise his own whims but is accountable to the will of the nation in the discharge of this responsibility. This was stated in a convincing manner by Henry L. Stimson, then Secretary of War, on the 13th of April, 1945: "I consider that the care of the sick and wounded and the character of the hospitalization in the Army are matters for the direct responsibility of the Secretary of War; also that the Surgeon General should be his principal adviser in regard to these vital matters" (14). This principle has been reaffirmed by Mr. Stimson's successor, Secretary Robert Patterson, and is a challenge not only to the Surgeon General but to the medical profession.

There were many lessons of the first World War that were promptly forgotten, or the significance of which at the time were really not appreciated. In looking back at the experience of World War I with the perspective of the recent war, there is no single item that has more profound significance than the position occupied by Franklin H. Martin as the representative of the medical profession during the first conflict. It contrasts with the lack of a medical statesman at that level in World War II. On October 11, 1916, President Woodrow Wilson appointed Franklin H. Martin to the Advisory Commission of The Council Of National Defense. The story is graphically told by the pen of Dr. Martin (17) himself in his *Digest of the Proceedings of the Council of National Defense during the World War*. Representation of the profession in an advisory capacity at the Cabinet level insured that the voice of Medicine could be heard.

In this respect I would be remiss not to pay sincere and deserved tribute to our own Dr. Fred W. Rankin. Without the strategic advantage of position granted to Dr. Martin in World War I, it was inevitable that General Rankin's well designed efforts should meet with frustration time and time again. Nevertheless, by skillful and untiring efforts as Chief Surgical Consultant he stands out as the Sponsor of the American Surgeon, A.U.S., and the cornerstone upon which the achievements of American Surgery in World War II were erected.

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PENICILLIN—ITS USE IN SURGERY AND INFLUENCE ON EARLIER TYPES OF CHEMOTHERAPY

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SINCE the days of Ancient Greece, surgery has advanced largely through contributions made by the various basic sciences. Thus philosophy, anatomy, pathology, physiology, bacteriology, and biochemistry have each aided in its development. With the advent of the bacteriological era and establishment of the bacterial concept of infections, the attention of surgeons and bacteriologists was directed to the discovery of chemical bactericidal agents which would control infection by destroying the bacteria in the tissues. Many were found that killed bacteria *in vitro* even in high dilutions, but the very qualities which made them bactericidal also caused them to be toxic to human tissues, usually producing redness, swelling, induration, delayed healing, and often an increased incidence of infection. This was so universally true that as late as 1935 the goal of chemotherapy was still a dream in the minds of surgeons. At this time, however, the preliminary work had already been done which was to permit the realization of this dream through the development of the sulfonamides and penicillin and to open the present or chemotherapeutic period in surgery. Although some progress had been made prior to 1935 in the control of infections by the action of chemical agents, it was limited to specific agents for a few diseases caused by micro-organisms other than bacteria, such as the arsenicals for syphilis and ratbite fever, and quinine for malaria. Thus the actual onset of practical chemotherapy for bacterial infections was in 1935 when Domagk introduced prontosil.

Sulfanilamide, which was subsequently found to be the active ingredient of prontosil, has had a profound effect upon the practice of surgery. Its derivative, sulfadiazine, has proved to be the least toxic for systemic administration and the sulfonamide of our choice in surgical infections. Although its correct use has revolutionized the management of many infections, it has also been frequently misused. Not only have all types of infection, diagnosed and undiagnosed, been treated, but its inadequately controlled administration has caused unnecessary toxic reactions giving rise to a false impression among some surgeons that sulfadiazine is too dangerous for practical use. It seems advisable therefore to consider briefly the prophylactic and therapeutic indications for sulfonamide therapy in surgical conditions.

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PROPHYLAXIS

Experimental and clinical experience (17) has shown that the systemic or local use of the sulfonamides will not prevent the development of local infection in contaminated wounds, but there is definite evidence that systemically administered sulfadiazine keeps infection that develops within the wound more localized and thereby prevents invasive infection. In addition, we have gained the impression that local infections developing under systemic sulfadiazine therapy were often attenuated, developing more slowly and responding to treatment more readily.

In penetrating wounds of the abdomen, the prophylactic value of the sulfonamides has been more obvious as was shown in a comparison (1) between a group of 161 cases treated with prophylactic sulfonamide therapy, operation, and supportive measures and another group of 104 similar cases treated without sulfonamide therapy.

Although massive hemorrhage, particularly from the aorta and vena cava, and pneumonia have remained serious causes of death, the incidence of fatal peritonitis and severe shock has been significantly reduced. Before the use of sulfonamide therapy, peritonitis was responsible for 31.0 per cent of the deaths in this series, while it was a contributing cause of

TABLE I.—COMPARISON OF THE INCIDENCE OF THE CAUSES OF DEATH IN PENETRATING WOUNDS OF THE ABDOMEN BEFORE AND AFTER CHEMOTHERAPY

151 cases admitted between January, 1938 and January, 1942.			161 cases admitted between January, 1942 and May, 1946.		
		Per cent			Per cent
Mortality rate.....		27.9	Mortality rate...		11.6
Causes of death	Cases no.	Per cent	Causes of death	Cases no.	Per cent
Peritonitis.....	9	31.0	Hemorrhage	7	30.4
Hemorrhage...	7	24.1	Pneumonia.	4	17.4
Shock.....	6	21.3	Putrefactive empyema.	4	17.4
Pneumonia....	5	17.2	Peritonitis..	2	8.7
Uremia.....	1	17.2	Meningitis..	2	8.7
Retroperitoneal cellulitis.....	1	3.4	Uremia.....	1	4.3
			Undetermined.	1	4.3

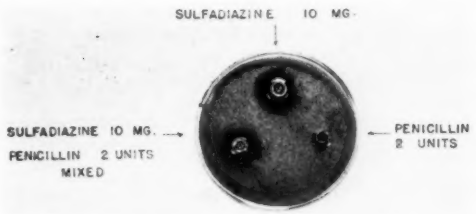

Fig. 1. Blood agar plate showing the superior bacteriostatic effect *in vitro* of sulfadiazine over that of penicillin on a mixed culture of both gram negative and gram positive bacteria. Pseudomonas aeruginosa; Staphylococcus aureus, resistant to penicillin; Escherichia coli; Streptococcus viridans, resistant to penicillin; hemolytic streptococcus, susceptible to penicillin; Staphylococcus aureus, susceptible to penicillin; nonhemolytic streptococcus, resistant to penicillin.

death in only 2 instances in the patients treated with sulfonamides. There is also evidence that systemic sulfadiazine therapy has had a similar beneficial effect in operations for resection of the bowel by greatly reducing the incidence of postoperative peritonitis.

THERAPEUSIS

The value of sulfonamide therapy has been unquestionably established in acute infections produced by a hemolytic streptococcus, the pneumococcus, and the gonococcus, but it is of little or no value in those caused by the hemolytic staphylococcus (2, 4, 12, 13, 18). Its advantages of low cost, ease of administration, and high bacteriostatic action often make it the drug of choice in these infections.

Sulfadiazine is still a valuable drug in certain mixed infections produced by various gram negative and gram positive bacteria of the intestinal tract. *In vitro* studies on examples of mixed bacterial florae show that its marked bacteriostatic action is usually superior to that of penicillin in the usual concentrations which are built up in the blood during systemic therapy (Fig. 1). Clinical experience has likewise demonstrated the effectiveness of this form of chemotherapy in mixed infections. More recently very large doses of penicillin have proved to be very effective in the management of mixed infections. However, certain limitations of sulfonamide therapy have become increasingly apparent, including (1), the presence of bacterial species and group resistance; (2) the inactivation of bacteriostatic activity by inhibitors found in pus, wound exudates, and necrotic tissue; (3) the development of drug fastness by many of the infecting bacteria; (4) the occurrence of some toxic reactions when its administration was not carefully controlled; (5) its inability to penetrate areas of pus and necrosis, and (6) the occasional occurrence of drug idiosyncrasy.

With the introduction of penicillin, many of these limitations have been overcome. The sulfonamide inhibitors have little or no effect on the bacteriostatic action of penicillin and its extremely low toxicity has been of equal significance. Doses of one million units every 3 hours have been used repeatedly, and in one instance a child received 100,000,000 units each 24 hours for 2 weeks without evidence of toxicity (13). The toxic reactions that have occurred during penicillin therapy have been due largely to impurities or idiosyncrasies, and the threshold of toxicity as yet is undetermined.

At the present time, penicillin is the most effective chemotherapeutic agent available for the treatment of many surgical infections, particularly those caused by the staphylococci, the aerobic streptococci, the gonococci, and the anaerobic streptococci. Evidence of its superiority over the various sulfonamides in the therapy of staphylococcal infections is overwhelming, and its effectiveness in infections caused by sulfonamide-resistant strains of the streptococcus and gonococcus have been outstanding. The micro-organisms sensitive to its action *in vitro* are listed in Table II and

TABLE II.—PENICILLIN ACTIVITY IN VITRO—SENSITIVE MICRO-ORGANISMS

Gonococcus	Clostridium histolyticus
Meningococcus	Clostridium septique
Streptococcus	Clostridium sordelli
hemolytic	Clostridium oedematiens
viridans	Clostridium sporogenes
microaerophilic	Clostridium bifermentans
anaerobic	Bacillus diphtheriae
Staphylococcus	Bacillus pseudodiphtheriae
aureus	Lactobacillus
albus	Crytococcus hominus
anaerobic	Spirillum minus
Micrococci	Streptobacillus moniliformis)
Pneumococcus	Treponema pallidum
Bacillus subtilis	Bacillus alkaligenes (some strains
Bacillus anthracis	Leptospira icterohemorrhagiae
Actinomyces bovis	Erysipelothrix rhusiopathiae
Clostridium tetani	
Clostridium tetanomorphum	
Clostridium botulinum	
Clostridium welchii	

those resistant in Table III. More recently the very low toxicity of penicillin has permitted exploration of the clinical value of very large doses in infections produced by bacteria resistant or slightly susceptible to its action. The encouraging results obtained justify a more thorough investigation of the therapeutic possibilities of large doses up to one million or more units every 3 hours in this type of infection.

In the 4 years between November, 1942, and November, 1946, 704 surgical infections treated with penicillin, surgery when indicated, and the general and local supportive measures for correction of altered physiology have been studied and they included the following:

Staphylococcal infections	427
Pneumococcal infections	70
Anaerobic streptococcal infections	22
Aerobic streptococcal infections	89
Gonococcal infections	46
Actinomycotic infections	17
Human bite infections	9
Ratbite fever infections	8
Gas gangrene infections	12
Pyodermia gangrenosa infections	4

Experience has shown that penicillin is the chemotherapeutic agent of choice in the treatment of all staphylococcal infections in surgery, having replaced all previous forms of chemotherapy. An arbitrary tabulation of the clinical results obtained with penicillin in the treatment of the 427 cases with established staphylococcal infections is given in Table IV.

TABLE III.—PENICILLIN ACTIVITY IN VITRO.—RESISTANT OR SLIGHTLY SUSCEPTIBLE STRAINS OF MICRO-ORGANISMS

Bacillus coli	Acne bacillus
H. influenzae	M. tuberculosis
Bacillus typhosus	Bacillus tularense
Bacillus paratyphosus	Brucella melitensis
Bacillus dysenteriae	Brucella abortus
Bacillus proteus	Bacillus melaninogenicum
Bacillus enteritidis	Monilia albicans
Bacillus pyocyaneus	Monilia candida
Aerobacter aerogenes	Blastomyces
Bacillus fluorescens	Toxoplasma
Bacillus friedlanderi	Bacillus mycoides
Bacillus prodigiosus	Lymphopathia venereum virus
Bacillus pestis	
Vibrio cholerae	

The effects of penicillin therapy were particularly apparent in the treatment of the severe staphylococcal infections with invasive manifestations. If the infection was in the diffuse or cellulitic stage, penicillin therapy was often followed by complete and spontaneous resolution and a minimal amount of local destruction of tissue (Fig. 2). If the diagnosis

TABLE IV.—RESULTS IN PENICILLIN THERAPY STAPHYLOCOCCAL INFECTIONS

Clinical Diagnosis	No. cases	Results			
		Excellent	Good	Questionable	Failure
Septicemia	50	21	15		14
Carbuncles	51	24	24	2	1
Cellulitis	49	31	16	1	1
Furunculosis	29	23	4	2	0
Acute hematogenous osteomyelitis	60	28	29	2	1
Chronic osteomyelitis	54	9	24	12	9
Infected wounds	52	31	16	1	4
Abscess	14	8	6		
Hand infections	21	16	3	2	
Abscesses of lung	13	5	2		6
Brain abscess	2	1			1
Bursitis	6	5	1		
Postoperative parotitis	6	4	2		
Chronic lymphadenitis with lymphedema	4		4		
Abdominal sinus	4		1		3
Hydradenitis suppurativa	9	7	2		
Pericarditis	2	1	1		
Spinal epidural abscess	1		1		

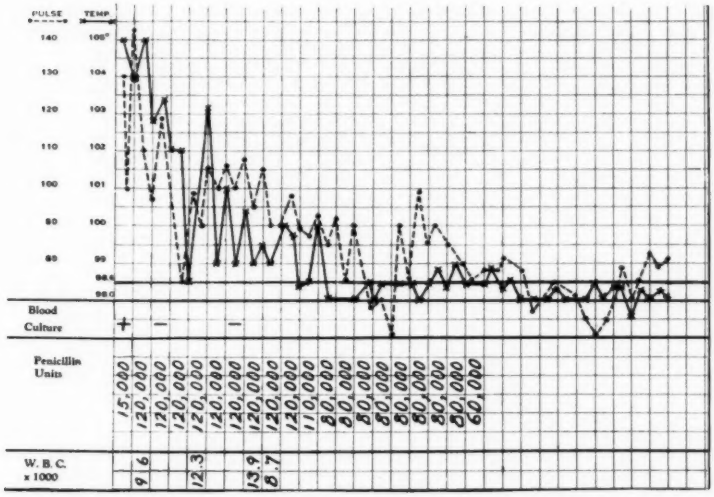

Fig. 2. J. S., aged 11 years: acute hematogenous osteomyelitis of right tibia with bacteriemia. The chart illustrates the usual type of response of an invasive staphylococcal infection with bacteriemia when diagnosed and treated early before the development of metastatic complications.

was made late, however, the invasive qualities of the infection were overcome and the process was localized, but necrosis of tissue usually occurred. Frequently, penicillin so controlled the invasive qualities of staphylococcal infections that emergency radical surgical decompression or excision of infected areas often was eliminated or replaced by more conservative local types of surgery.

Early diagnosis was of considerable importance in determining the results obtained with penicillin chemotherapy in regard to morbidity, mortality, and functional results. Accurate or complete clinical, as well as bacteriological, diagnosis was likewise of definite importance. The presence of secondary or metastatic infectious complications usually delayed or prevented the complete response to chemotherapy (Fig. 3). Failures were associated with infections in the aged, severe conditions produced by penicillin-fast staphylococci, overwhelming infections in patients moribund before the start of penicillin, incomplete diagnosis, or the presence of endocarditis.

A more accurate impression of the value and limitations of penicillin in the management of staphylococcal surgical infections can be obtained from an analysis of its effect on staphylococcal septicemia, carbuncles, acute hematogenous osteomyelitis, chronic osteomyelitis, and acute postoperative parotitis.

Staphylococcal septicemia. The intelligent use of penicillin has significantly reduced the high mortality and prolonged morbidity of staphylococcal septicemia. In the past the circulating bacteria were filtered out of the blood by the reticuloendothelial system, and subsequently often produced secondary or tertiary metastases in the viscera even when surgical attack removed or seemed to control the primary distributing focus. Because the metastatic abscesses were frequently multiple and often inaccessible to surgery, the patients surviving the initial primary infection frequently succumbed to the later infectious complications. For these reasons and our lack of any method of controlling the staphylococcus in remote or unknown areas, the mortality of established staphylococcal septicemia was very high, varying between 60 and 90 per cent in various series, and averaging 79 per cent. When the infection spread to the meninges or became engrafted upon heart valves, the mortality approached 100 per cent.

TABLE V.—STAPHYLOCOCCAL SEPTICEMIA

	40 Cases treated with sulfadiazine, bacteriophage, etc. 1940–1943 Per cent	50 Cases treated with penicillin 1943–1946 Per cent
Mortality	67.6	30.0
Recovery	32.5	70.0
	Morbidity	
	Hospital days	Hospital days
Fatal Cases	18	22.8
Recovered Cases	80	53.8

TABLE VI.—FATAL CASES OF STAPHYLOCOCCAL SEPTICEMIA

Diagnosis	No. of cases
Vegetative endocarditis	6
Pneumonia	3
Infected burns of 60 per cent body surface	1
Cavernous sinus thrombosis	1
Otitis media with lateral sinus thrombosis	1
Pemphigus	1
Acute osteomyelitis (terminal)	1

The obvious values and limitations of penicillin therapy in the management of this condition are illustrated in a recent study of 90 cases of hemolytic staphylococcus septicemia at the Cincinnati General and neighboring hospitals between 1940 and 1946. A total of 40 cases of staphylococcus septicemia were treated with sulfonamides, surgery when indicated, or bacteriophage, between 1940 and 1943, and a similar series of 50 cases were treated with penicillin in addition to other medical and surgical medical measures between 1943 and 1946. Table V compares the two series in respect to mortality and morbidity, indicating the profound effect penicillin has had upon this infection.

It is apparent that penicillin has approximately reversed the mortality and recovery rates. Whereas only 32.5 per cent recovered under sulfonamide, bacteriophage, and other forms of therapy, 70 per cent recovered under penicillin therapy. A further analysis of the fatal cases reveals some of the limitations of penicillin therapy (Table VI).

The results in the cases developing vegetative endocarditis, particularly early in the series, were very poor, and this condition accounted for almost half of the deaths. Of the remaining 8 fatal cases, 5 of the deaths occurred within 12 to 48 hours after their admission to the hospital and start of penicillin treatment. In these instances, the fulminating infection or moribund condition of the patient produced death before the maximum chemotherapeutic effect could become manifest. In the case of the infected burn, the Staphylococcus aureus was resistant to the action of penicillin.

The outcome in the individual case was dependent upon many factors (2, 12), including the age of the patient, the susceptibility of the strain of staphylococcus to penicillin, the site and nature of the primary infection, the duration of the bacteriemia, the presence and location of secondary or metastatic abscesses, the accessibility of the primary or secondary infections to surgical drainage, and the presence of other associated and complicating diseases. Inadequate treatment predisposed to relapse. Experience has shown that treatment is most successful in young adults or children in whom the diagnosis of staphylococcal bacteriemia is made early, penicillin therapy given early and intensively, and surgical drainage is possible when indicated.

Carbuncles. A carbuncle is essentially a spreading and necrotizing staphylococcal infection of the deeper layers of the skin and subcutaneous tissue which may result in extensive necrosis, sloughing, liquefaction of the subcutaneous tissue, septicemia, and death. The many forms of treatment which have been devised for carbuncles are an indication of our inability to control the locally or generally invasive characteristics of this infection. The great majority of surgeons have learned to employ crucial incisions or excision and because of the tendency of carbuncles to extend locally or invade the general circulation, the treatment of choice at many clinics, including the Cincinnati General Hospital, has been radical excision. Sulfonamide therapy in general has been disappointing due principally to the natural resistance of the hemolytic Staphylococcal aureus.

The marked effect of penicillin on the management of carbuncles is shown in a group of 40 cases with carbuncle which we have treated with penicillin between February, 1944, and October, 1946, 8 of which received both penicillin and sulfadiazine. The dosage employed was 15,000 to 20,000 units every 3 hours given intramuscularly in every instance but one in which it was given intravenously. The average

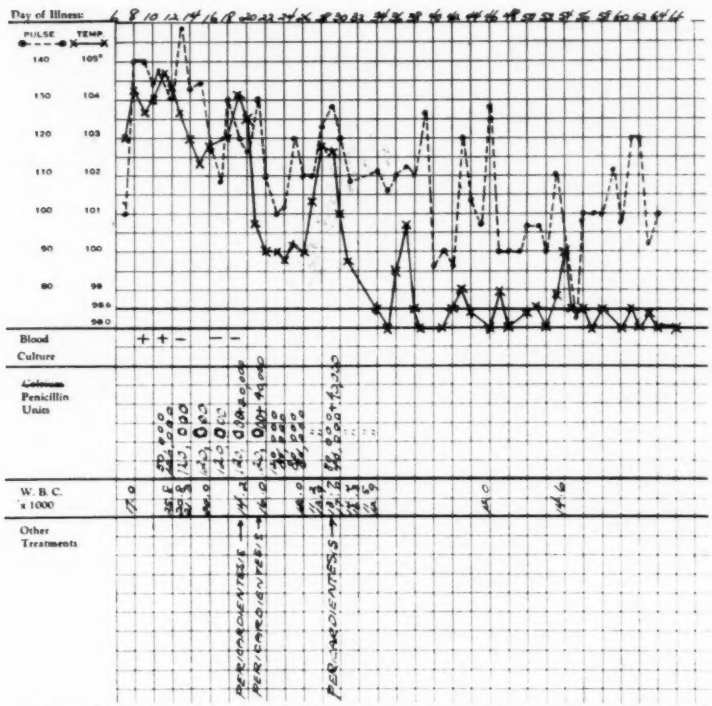

Fig. 3. J. B., aged 8 years: acute hematogenous osteomyelitis with bacteriemia and metastatic pericarditis. Chart shows failure of response to penicillin therapy until metastatic infectious complication in the form of a pericarditis is recognized and treated as indicated.

total dose was 927,000 units and the average duration was 7 days.

The results of treatment indicate that penicillin is obviously the chemotherapeutic agent of choice in this type of infection. When given early, in sufficient amounts, and over a long enough period of time, it brought the general and local invasive manifestations under control within a period of 48 to 72 hours, and so modified the subsequent course that both mortality and morbidity were reduced. In our experience, penicillin therapy was followed by complete and spontaneous resolution in 26.5 per cent of the cases (Figs. 4 and 5), by partial resolution with centralized necrosis in 22.4 per cent of the cases, with partial resolution and abscess formation in 49.0 per cent of the cases, and by failure in 2 per cent of the cases. Thus it was not necessary to subject these patients to emergency total excision of the lesion in order to control this infection. Since the invasive qualities have been controlled so effectively with penicillin, more limited surgical procedures are recommended when indicated consisting of incision and drainage of abscesses occurring during therapy and cruciate incision for the removal of necrotic tissue.

Acute hematogenous osteomyelitis. In the past, the results of treatment in this condition have been unsatisfactory for several reasons. Difficulties in diagnosis often resulted in delay and spread of the process with extensive destruction of the bone. When early diagnosis

TABLE VII.—RESULTS OF PENICILLIN THERAPY

	Cases	Per cent
1. Spontaneous resolution	13	26.5
2. Partial resolution with necrosis	11	22.4
3. Abscess formation	24	49.0
4. Failure	1	2.0

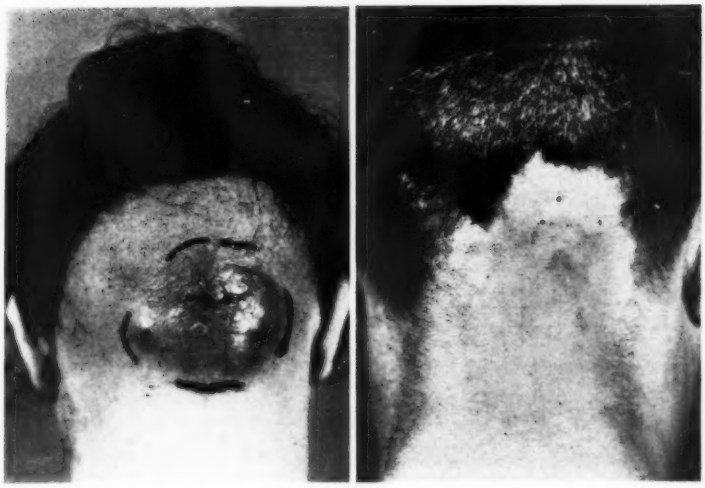

Fig. 4. E. H., aged 43 years, admitted to Cincinnati General Hospital, August 2, 1944, with a large carbuncle of the neck of 10 days' duration. Temperature and pulse remained normal after the third day. a, left, Appearance of carbuncle on August 3, 1944, at start of treatment with penicillin; b, August 12, 1944, disappearance of the carbuncle and almost complete healing have occurred in 9 days.

was made, the principal method of arrest and control of the necrotizing process was emergency decompression of the involved area by surgical drainage followed by prolonged periods of immobilization. More recently, chemotherapy with the sulfonamides used as a supplement to surgical intervention aided in the control of the infection, but left much to be desired. Penicillin, on the other hand, has had a profound effect upon acute hematogenous osteomyelitis and has greatly modified both its management (8, 14, 19) and roentgenographic interpretation (9). In the group of 64 cases of acute hematogenous osteomyelitis treated with penicillin, the mortality rate was remarkably low, being 1.5 per cent. In general, the other results of penicillin therapy varied primarily with the time of diagnosis and start of treatment, falling into 4 groups.

The first group included those cases in which the correct diagnosis was made within the first 3 or 4 days, and adequate treatment was started immediately. The results were truly excellent, surgical intervention usually being unnecessary and abscess formation infrequent. After a period of 36 to 72 hours, the fever, rapid pulse, bacteriemia, and other general signs of the severe infection began to disappear. At the end of a week the temperature was usually normal and the patient looked and felt quite well. The local signs of infection, such as tenderness, edema, and redness, also began to recede after a similar latent period. During the next 1 to 6 months a series of roentgenographic changes occurred in the involved bone which were minimal, consisting of localized periosteal reaction or small areas of patchy decalcification of the underlying cortex, or both. These findings occasionally were hard to see and could be easily overlooked.

In the second group in which the diagnosis and treatment with penicillin were moderately delayed for 4 to 7 days, the general and local infections were brought under control by penicillin less promptly after a period of 2, 3, or more days during which little or no clinical response was evident. Localized soft tissue abscesses occasionally developed and when small, they were successfully treated by aspiration and local injections of a solution of penicillin. When large, surgical drainage by incision was done to minimize further tissue destruction by the accumulated necrotizing bacterial toxins. If surgical drainage was insti-

Fig. 5. V. L., aged 33 years. a, left, Carbuncle of face with diffuse cellulitis, thrombophlebitis of facial, external, and anterior jugular veins, staphylococcal bacteriemia, and bilateral pneumonia. Temperature, 106 degrees F., at start of penicillin therapy. b, Effect of 10 days' therapy with penicillin.

tuted, the fall of temperature was usually prompt and not delayed for 36 or more hours as in the case treated without surgical intervention.

After a week or more had elapsed, periosteal reaction and localized patchy demineralization of the underlying metaphysis became evident in the roentgenograms and increased in extent and degree, becoming most marked 1 to 5 months after the onset of the infection. Recalcification of the demineralized areas followed with re-establishment of a more normal appearance of the bone. Sequestration rarely occurred in this group.

The third group included cases in which the diagnosis and treatment were delayed for 7 to 10 or more days and those in which the infection was unusually severe. The local destruction of bone became very great and soft tissue abscess formation and sequestration occurred in most, but not all, of the cases. The local infection was arrested with more difficulty in this type of case and longer periods of treatment with penicillin were usually required. Small abscesses were treated by aspiration and large ones by incision and drainage. Prolonged immobilization by cast in these cases seemed to be definitely indicated.

The bony changes as revealed by serial roentgenograms at the start of penicillin treatment showed extensive bone destruction which increased on subsequent examinations. Sequestration occurred in most cases and in many instances the smaller sequestra were gradually absorbed spontaneously.

The fourth group included certain fulminating infections in which the patient would not live 48 or more hours to permit the maximum effect of penicillin. Surgical intervention after adequate preoperative preparation was necessary as an emergency measure in addition to intensive penicillin therapy.

In general the effects of penicillin included control of the generalized infection with sterilization of the blood stream, reduction of the mortality rate, and decrease in the incidence of metastatic or secondary infectious complications. If metastatic complications, such as staphylococcal pneumonia, pleuritis, pericarditis, thrombophlebitis, etc., already existed, penicillin was a powerful chemotherapeutic agent aiding in their control as an adjunct to surgical or conservative treatment as indicated. Thus the morbidity was also decreased.

There seems to be little doubt that adequate penicillin therapy can eliminate the necessity of emergency surgical intervention in most cases of early acute hematogenous osteomyelitis (8, 14, 19). It must be emphasized that early diagnosis can be made only on clinical grounds and that little or no help is to be expected from the roentgenograms for 10 or more days. If there is any doubt as to the presence of an acute osteomyelitis, it is better

Fig. 6. M. K. a, left, Severe acute hemolytic streptococcal cellulitis of face, neck, and scalp with gangrene which was resistant to sulfonamide therapy. Temperature was 105 degrees F. at start of penicillin therapy. b, Appearance of lesion after control of infection, separation of slough, and preparation of area for skin graft.

to start penicillin therapy rather than wait until the diagnosis is proved.

Of particular interest were the resultant roentgenographic changes which occurred in the involved bone treated with or without surgery. During the period of penicillin therapy, evidence of bone damage was absent or confined to minimal changes such as slight periosteal reaction or small areas of demineralization in the underlying cortex. After the cessation of chemotherapy, the periosteal reaction and mottled appearance of the underlying bone progressively increased, reaching a maximum 1 to 5 months after the onset of the infection. In this way the bone always looked worse a month or more after penicillin therapy than during it. This picture has been interpreted as being the result of spontaneous absorption of bone destroyed early in the infection, and not as the result of continued destruction of bone by an extending chronic osteomyelitic process. Following this, recalcification of the involved areas occurred, often very rapidly. Meanwhile normal growth of the metaphyses, calcification of the adjacent epiphyses, and return of function occurred. These facts suggested that adequate penicillin therapy may sterilize the infected bone converting an area of septic necrosis to one of aseptic necrosis. One of the most important aspects of this problem remains unanswered as yet, the question as to whether or not the infection has been completely cured.

Chronic osteomyelitis. In chronic osteomyelitis the results were usually disappointing unless penicillin therapy was used in conjunction with radical surgery. Spontaneous resolution of an acute exacerbation was noted in only 9 instances. In the remainder surgery was necessary along with penicillin to clean up the local infective process.

Acute secondary or postoperative parotitis. The control of acute secondary parotitis by chemotherapy is desirable since its arrest by conservative measures is uncertain and its control by surgical incision and drainage has certain disadvantages. Incision may result in unsightly scars, occasional injury to the facial nerve, salivary fistulas, or troublesome secondary infection (5). In addition, a general anes-

TABLE VIII.—AEROBIC STREPTOCOCCAL INFECTIONS—RESULTS OF PENICILLIN THERAPY

Clinical diagnosis	No. Cases	Results			
		Excellent	Good	Questionable	Failure
Septicemia	26	13	6	1	6
Cellulitis	16	12	4		
Acute hematogenous osteomyelitis	3	2	1		
Acute streptococcal gangrene	5	1	2	1	1
Meningitis	4		2	1	1
Empyema	3		2		1
Pericarditis	2	1			1
Peritonitis	3	1	2		
Liver abscess	3		1		2
Acute mastoiditis with lateral sinus thrombosis	2	1	1		
Septic abortion	23	19	2	2	

thetic and operation unquestionably throw an added burden upon the patient greatly weakened by some other primary disease which predisposed to the development of the acute parotitis. The simplicity of administration and the directness of action of effective chemotherapy largely obviate these disadvantages. Of 6 patients treated with penicillin, 4 underwent complete and spontaneous resolution. A fifth responded satisfactorily to penicillin after failing to respond to Lugol's solution. The sixth underwent partial resolution with the formation of an abscess which was incised.

The general response of this infection to penicillin therapy followed the general pattern seen in other surgical infections treated by chemotherapy. An interval of 24 to 48 hours following the start of treatment preceded the development of obvious signs of clinical improvement. Thereafter, the improvement was progressive and usually rapid.

Aerobic hemolytic streptococcal infections. While most of these infections respond promptly to sulfonamide therapy, penicillin is also very effective, and particularly valuable in those cases resistant to the sulfonamides (Fig. 6). The results of therapy in cases of hemolytic streptococcal infections treated at this Hospital, most of which were sulfonamide resistant, are summarized in Table VIII.

TABLE IX.—ANAEROBIC STREPTOCOCCAL INFECTIONS—RESULTS OF PENICILLIN THERAPY

Clinical diagnosis	No. cases	Results			
		Excellent	Good	Questionable	Failure
Bacteriemia	6	2	1	1	2
Septic abortion	9	2	6		1
Chronic burrowing ulcer	5		2	3	
Chronic progressive cutaneous gangrene	2			1	1

In the treatment of anaerobic streptococcal infections, penicillin was far superior to the sulfonamides (3). *In vitro* studies showed its bacteriostatic action under anaerobic conditions for the anaerobic streptococci to be far greater than that of the sulfonamides. We have had an opportunity to use penicillin therapy on 22 cases of anaerobic streptococcal infections and the results are shown in Table IX.

Pneumococcal infections. The average pneumococcal infections seen in surgical practice respond very well to sulfonamide therapy in much the same manner as do the hemolytic streptococcal infections. Penicillin therapy was therefore reserved for those cases which were sulfonamide resistant, and the results obtained in 70 cases are shown in Table X.

Tetanus. A clinical study (6) of 22 cases of established generalized tetanus seen in and about Cincinnati has failed to show evidence of any beneficial effect of penicillin on the course of this disease. There was no obvious

TABLE X.—SULFONAMIDE RESISTANT PNEUMOCOCCAL INFECTIONS—RESULTS OF PENICILLIN THERAPY

Clinical diagnosis	No. cases	Results			
		Excellent	Good	Questionable	Failure
Bacteriemia	33	20	4		9
Empyema	18	2	8	2	6
Meningitis	9	2	2		5
Arthritis	2		2		
Pericarditis	1				1
Abscess of neck	4	1	3		
Acute hematogenous osteomyelitis	1	1			
Peritonitis	2	1	1		

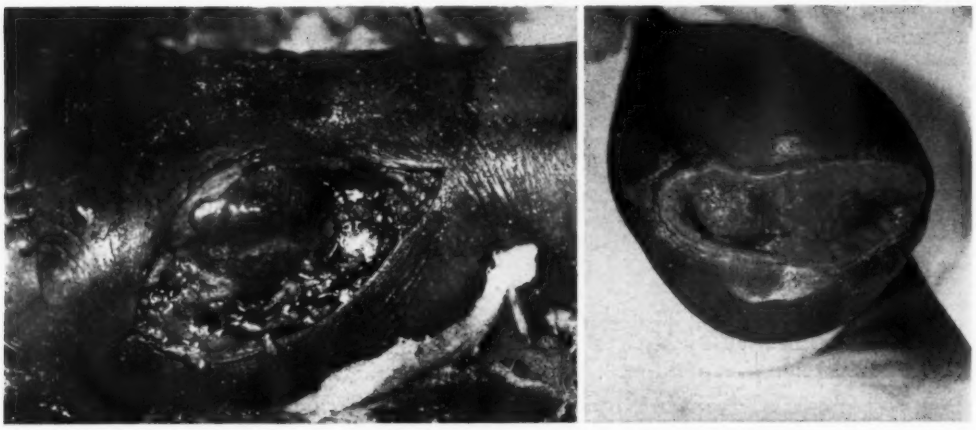

Fig. 7. G. B. a, left, Severe case of gas gangrene complicating compound fracture of tibia and fibula. Infectious process had produced complete gangrene of leg distal to wound and had spread through thigh to inguinal region. Treatment consisted of midthigh guillotine amputation penicillin parenterally, zinc peroxide topically, and serotherapy. b, Appearance of amputation wound above level of amputation has been brought under complete control.

fall in the temperature or pulse rate as has been repeatedly seen in other infections susceptible to its action, no decrease in mortality or morbidity, nor any definitive decrease in the severity, duration, or frequency of the convulsive seizures which could be attributed to the action of penicillin. Exceptions were found in cases complicated by pneumonia or other secondary infections susceptible to penicillin in which the improvement that occurred was due to the effect of penicillin on the complicating infection and not on tetanus. The evidence indicates that the successful management of tetanus depends not on chemotherapy but on early diagnosis, adequate serotherapy for neutralization of free toxin, control of the convulsions and the administration of general supportive measures.

Human bite infections. When once established this type of infection has been controlled with considerable difficulty in the past. Its necrotizing burrowing characteristics have resulted in prolonged morbidity, extensive septic necrosis of the tissues including bone, toxemia, impaired function, and even amputation. The results with penicillin therapy in 9 cases have been very promising, and they indicate that penicillin is a valuable therapeutic agent for this condition, being superior to the sulfonamides. In 5 of the cases the response to parenteral penicillin therapy, rest, immobilization, and elevation was excellent, the infection subsiding quickly and spontaneously with little or no evidence of residual infection or damage. The response was good in 3 other cases when penicillin was used in conjunction with incision and drainage, and questionable in the remaining infection.

Ratbite fever. Ratbite fever is essentially an invasive wound infection of two clinical types, (1) soduku caused by the Spirillum minus and (2) the septicemia form produced by Streptobacillus moniliformis (10). The endemic Japanese form, soduku, has responded to arsenotherapy but no satisfactory form of treatment was known for the streptobacillary type. The first 4 cases of ratbite fever caused by the Streptobacillus moniliformis which were treated with penicillin were studied at the Cincinnati General Hospital. The results of penicillin therapy in these 4 cases were excellent in 3 with sterilization of the blood stream, early fall in temperature and pulse, disappearance of rash and arthritis, and shortening of the course of the disease. In addition, studies *in vitro* indicated that penicillin has a powerful bacteriostatic effect on the Streptobacillus moniliformis.

Gas gangrene. Penicillin is by far the chemotherapeutic agent of choice in the control of

established gas gangrene. Clinical investigations indicate that parenteral penicillin used in conjunction with surgery gives encouraging results, but only when it is given in relatively large doses of 200,000 to 400,000 units and 800,000 units per day (11, 16, 18). In a study of experimental gas gangrene (7), the therapeutic value of penicillin has been determined quantitatively.

Average doses of penicillin had no measurable effect, but large doses corresponding to approximately 1,000,000 units given every 3 hours had a very definite effect, reducing the mortality, prolonging the life of the guinea pigs and localizing the lesions. Without surgery, however, discontinuation of penicillin was followed by prompt spread of the lesion and ultimate death. These experiments indicate clearly that penicillin in large doses is a valuable adjunct to adequate surgery in the treatment of established gas gangrene since it limits the spread of the lesion, prolongs the period during which surgical decompression and excision of involved muscles can be done successfully, and reduces mortality. This corresponds to the clinical impression of Jeffrey and Thomson obtained in 33 cases of gas gangrene that penicillin can arrest the progressive myositis but that radical surgery is still the main factor in treating the disease. In our clinical experience of 12 cases of gas gangrene, the use of penicillin in conjunction with surgical decompression or amputation seemed to be of definite value in overcoming the invasive manifestations of the infection. If the diagnosis was made at an early stage while the gangrene was more or less localized and incipient, radical decompression of the involved fascial compartments by free longitudinal incisions and excision of the infected muscle usually resulted in the arrest of the process and the saving of the extremity. If the diagnosis was made late when the process was extensive and had caused irreversible gangrenous changes in the extremity implying loss of function of the limb, open amputation of the guillotine type or some modification became necessary (Fig. 7). At the present time it is inconceivable that any type of serotherapy or chemotherapy can replace good surgery in the treatment of gas gangrene.

Actinomycosis. Penicillin has been much more effective than the sulfonamides in the treatment of actinomycosis, but in our experience it is used most effectively in conjunction with sulfadiazine or sulfamerazine. Penicillin given in full doses over a prolonged period of at least 4 to 8 weeks in association with sulfadiazine which is continued under control for an additional 4 to 6 months has given us the best results. Very satisfactory results were obtained in the cervicofacial type, and other cases of both abdominal and thoracic actinomycosis have undergone arrest and rather spectacular regression under this management with progressive decrease in size and finally disappearance of the tumor masses and pain. Whether or not complete cures have been obtained in these cases remains to be seen.

SUMMARY

It is evident that the sulfonamides and penicillin are very effective and useful agents in the treatment of many infections commonly encountered in the practice of surgery. Penicillin is far superior to the sulfonamides in the treatment of infections caused by the staphylococcus and it has been particularly useful in the cases of infection caused by sulfonamide resistant gonococci, hemolytic streptococci, and pneumococci. It is also the chemotherapeutic agent of choice in gas gangrene, ratbite fever, actinomycosis, anaerobic streptococcal infections, and human bite infections. The use of increasingly large doses of penicillin, permitted by its very low toxicity, is gradually extending the field of effective chemotherapy in other infections produced by less susceptible bacteria. Penicillin has been strikingly effective in diffuse or generalized staphylococcal infections which have been diagnosed and treated early with penicillin, with the exception of those caused by a resistant strain or those complicated by acute vegetative endocarditis. The early treatment of diffuse infections caused by the staphylococcus or streptococcus often was followed by such prompt and complete arrest of the destructive bacterial process that suppuration did not develop and surgical intervention either became unnecessary or limited to more localized measures. In

the management of suppurating surgical infections caused by susceptible bacteria, penicillin therapy has had a striking beneficial effect on mortality and morbidity, but the fundamental surgical principles of early accurate diagnosis, early treatment, rest, adequate external drainage, correction of altered physiology, and vigilant supportive treatment remain as important as ever.

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CANCELLOUS BONE GRAFTS TO THE JAW

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THE problem of bone grafting in the lower jaw merits serious consideration even though it is met with infrequently in civilian practice. Distortion of appearance which results from mandibular loss in the course of surgery of malignancy and following severe infection or trauma is secondary in importance to disturbance of speech and to the impairment of mastication and deglutition, which affects profoundly the individual's entire nutritional status. In war surgery the necessity of bone grafting to the lower face arises rather commonly because of the high incidence of massive maxillofacial injuries from bullets and shell fragments.

Presented in the symposium on Plastic Surgery of the Head and Neck, before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–20, 1946.

Mandibular bone grafts were first employed 30 years ago during World War I by the German, French, and English-American groups of workers with perhaps a thousand cases re-

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b c d

Fig. 1. O. R. I., Pfc., age 21 years, received a shell fragment wound June 29, 1944, with loss of considerable soft tissue of the chin and bony loss of the symphysis and anterior half of the right body of the mandible. It was necessary to readjust soft tissues for better coverage before insertion of a bone graft, and a labioalveolar sulcus was created later by a stent graft in order that a functioning denture could be used. a, Appearance on admission. b, Roentgenogram showing bone loss. c, Interlocking cap metal splint for immobilization. d, Roentgenogram showing cancellous bone graft bridging the defect. e, Appearance following bone graft.

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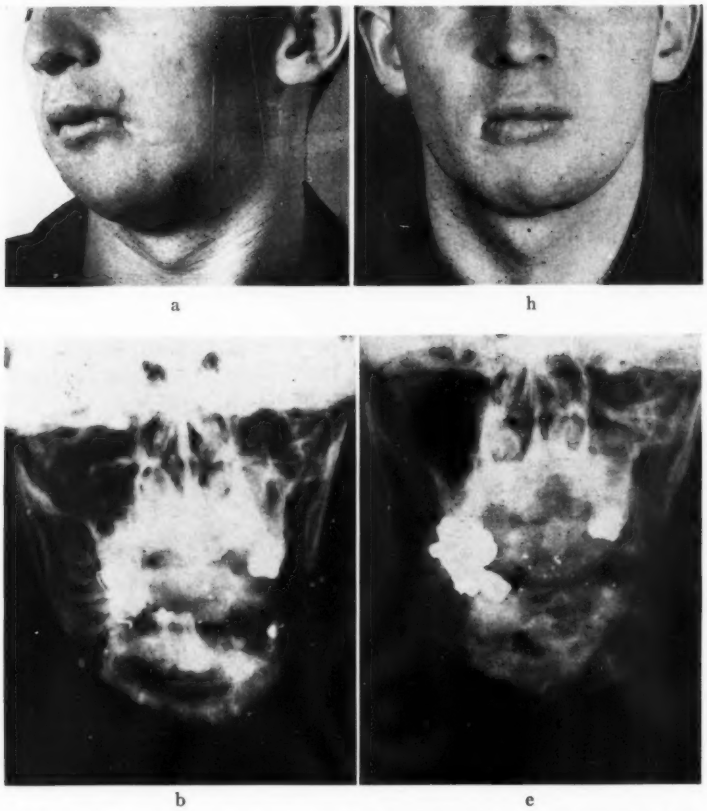


Fig. 2. B. N., Pvt., age 24 years, received a machinegun bullet wound of the face with loss of the greater portion of the left body and angle of the mandible, March, 1944. a, Appearance before operation after subsidence of reaction. b, Roentgenogram on admission showing large loss of substance on the left and nonunion on the right. c, Flange cap metal splint to maintain the fragment in normal position during the waiting period and at the same time allow function of the jaw. d, Interlocking cap metal splint, used for immobilization of the jaws at operation. e, Roentgenogram showing large cancellous bone graft in position. f, Stent graft to create sulcus for denture. g, Final denture before disposition. h, Final contour. (b-g are reproduced through courtesy of the J. B. Lippincott Company from article by Blocker.)

ported in all. A variety of sources were employed in the remedy of small losses of bone and in ununited fractures. These include:

1. Sliding or pedicle grafts from the mandible for losses not greater than 3 centimeters in the symphysis or body;

2. Cortical grafts from the tibia;

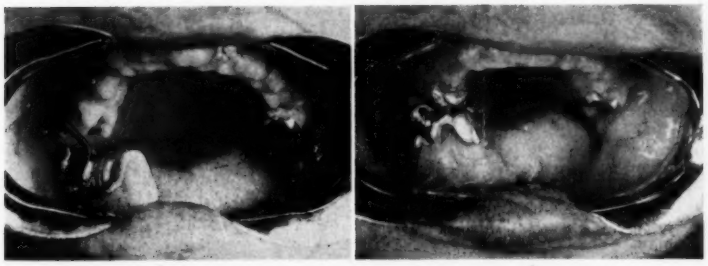
3. Osteoperiosteal grafts—thin shavings of bone and periosteum about 2 millimeters in thickness—for small bony defects not associated with disturbance of contour;

4. Rib grafts;

5. Clavicle grafts employed in pedicles from the neck for restoration of the symphysis and overlying soft structures of the chin;

6. Grafts from the ilium, particularly for large losses of bone and distortion of normal contour.

During recent years the use of iliac grafts has been the method of choice, although some workers, notably Barrett Brown, employ the rib whenever practicable.



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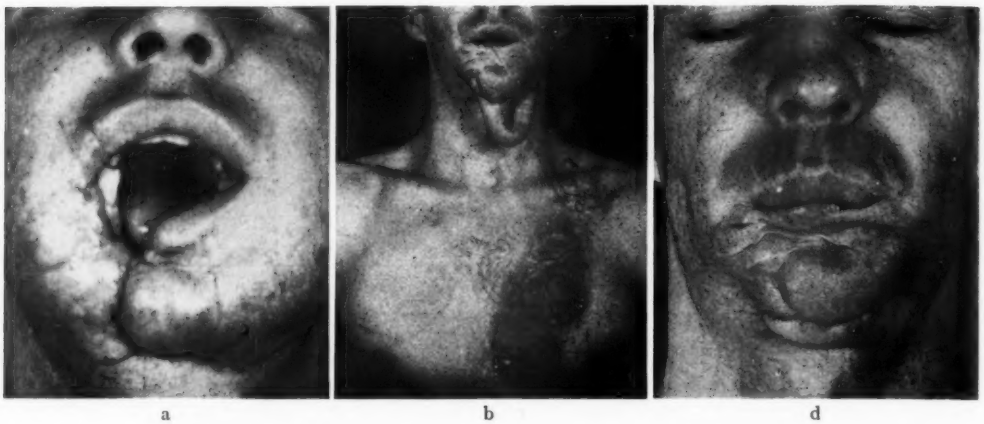
The literature on theories as to the mechanism of bone regeneration is voluminous and has influenced considerably the operative technique. For a long time it was felt that periosteum was indispensable, but experimental and clinical evidence has demonstrated that neither periosteum nor cortical bone is necessary for successful grafting. The superior qualities of cancellous or spongy bone provide for rapid vascularization and earlier stabilization and union; for this reason small chips of part-cortical part-cancellous bone are becoming increasingly popular in orthopedic and maxillofacial surgery when it is felt that immobilization can be maintained without the use of cortical bone as a splint for fragments. The employment of large blocks of pure cancellous bone from the ilium is the most recent innovation in bone grafting. And while other workers may be able to demonstrate equally good results with other methods of reconstruction of mandibular defects, we have found cancellous block grafts an extremely satisfactory medium of repair. The ilium is readily accessible and furnishes a large amount of available spongy bone. Following removal of all cortex the graft is easily cut and shaped to fit the requirements of the individual case. The use of chips alone is rather haphazard, and it is difficult to maintain good contour. For extensive defects, such as angle-to-angle loss of bone, we have employed at times a tantalum tray to give proper shape to the jaw. In these cases more than one block graft is used, and cancellous chips are packed around the open spaces.

With present-day dental applicances there need be no dependence on the mandibular graft for any part of fixation. Cancellous bone very quickly develops strength and evidence of firm bony union within 8 to 14 weeks' time after operation, when dentures may usually be fitted. We have been able to observe grafts directly 5 to 6 months after surgery when exposure is made to add a cartilage implant for improvement of chin contour. They show smooth white bone with a well-developed pseudoperiosteum and on stripping of this membrane, numerous nutrient vessels are seen entering the bone.

The most important requirements for success in bone transplantation are adequate sup-



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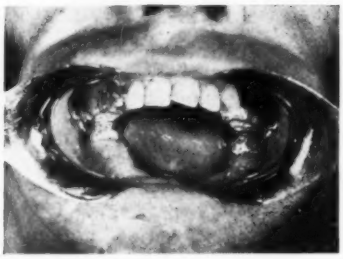

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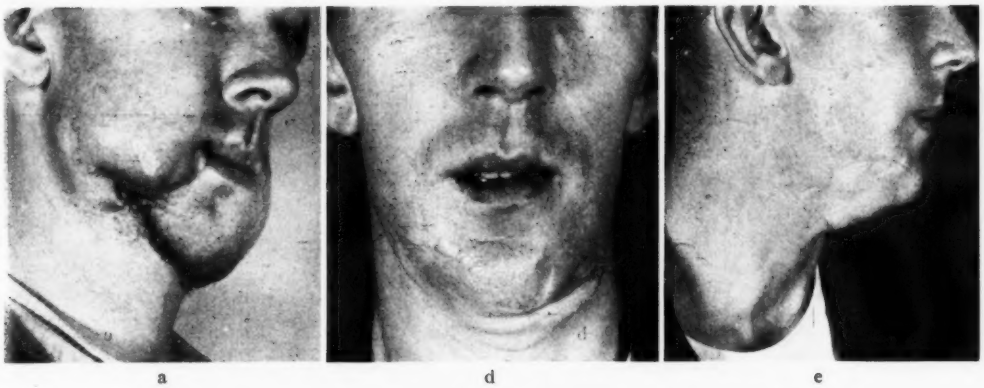
Fig. 3. V. A., Pfc., age 29 years, received a machine gun bullet wound of the face October 17, 1944, with avulsion of the soft tissues about the lower lip and floor of the mouth and loss of the symphysis and anterior half of each body of the mandible. a, Appearance on admission. b, Appearance following rearrangement of local tissues to stop the salival leak and raising of pedicle soft tissue from the chest to be used for reconstruction of the floor of the mouth prior to bone grafting. c, Interlocking cap metal splints for stabilization of the fragments. d, Appearance following bone graft.

ple cover, free of scar tissue and induration; absence of infection and avoidance of contamination at the time of operation; and proper preoperative and postoperative immobilization of fragments. The necessity of having resilient soft-tissue covering has not been adequately stressed, and here time is an inescapable factor in the elimination of wound reaction. For avulsion deformities pedicle flaps from the thorax and abdomen must be employed. Less severe defects may be taken care of by rotational flaps and other methods of rearrangement of local tissues. Even small adherent scars should be removed several weeks before bone grafting, with complete excision and wide undermining to give relaxation in closure. Operation should never be performed through a wide cicatrix or through an indurated area. Removal of loose sequestra and fragments of teeth hastens the subsidence of localized drainage and infection. We are not yet convinced that early operation is advisable even with the use of penicillin, and it has been our custom to delay bone grafting for a minimum period of 2 months following last drainage from the area. The great majority of our cases have waited over 6 months after subsidence of active evidence of infection.

Bone grafting to the jaw requires close cooperation of both surgeon and dentist. The dental surgeon assumes charge of all mechanical devices for immobilization of fragments before and at the time of operation and looks after the patient's oral and dental hygiene. Proper emphasis must be placed upon improvement of the general physical condition as well, with correction of anemia, weight loss, and protein imbalance.

The chief problem in individual bone graft procedures of the mandible is the method of fixation and immobilization to be employed. Various factors must be taken into consideration: size and character of the defect; position of teeth in the upper and lower jaw; and state



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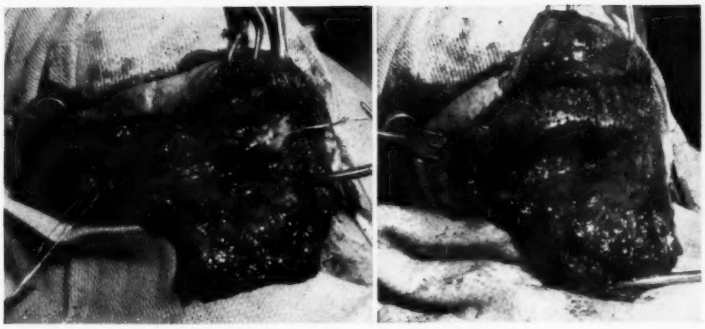

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Fig. 4. R. M. B., Corporal, aged 25 years, received a shell fragment wound June 19, 1944, with avulsion of soft tissues of the chin and floor of the mouth and loss of the right body and symphysis of the mandible. a, Appearance on admission showing granulations and draining sinuses. b, Exposure of mandibular defect at operation 1 year after admission. Soft tissue loss has been replaced with a pedicle flap from the chest. c, Tantalum tray containing cancellous block graft. d, Appearance following operation. e, Profile view.

of occlusion of the fragments. Because of the danger of opening into the oral cavity at the time of operation the position of fragments cannot be altered at that time except in angle defects or where the fragments are edentulous.

If both fragments are edentulous some modification of the Gunning splint is used during the waiting period and also following bone grafting. At operation we usually employ some type of internal fixation such as a piece of perforated tantalum shaped over an impression of a normal cadaver mandible.

Where one fragment is edentulous and the other contains teeth, the latter is kept in occlusion by a flange splint. The edentulous portion at operation is liberated on all surfaces, placed as nearly as possible into normal position, and maintained there by a wire through the angle tip or ramus which protrudes through the skin and attaches to a bar coming around the face from the intraoral splint.

Where both fragments contain teeth a cap metal splint with rigid crossbar is very satisfactory preoperatively. At the time of insertion of the graft two interlocking cap metal splints are used to hold the jaws absolutely immobilized. At the time of operation we have employed either endotracheal anesthesia or a combination of (1) high bilateral intraoral mandibular block with 2 per cent novocain, (2) local novocain infiltration, and (3) spinal anesthesia for removal of bone from the ilium. We prefer the second method because of the advantage of novocain-adrenalin solution in

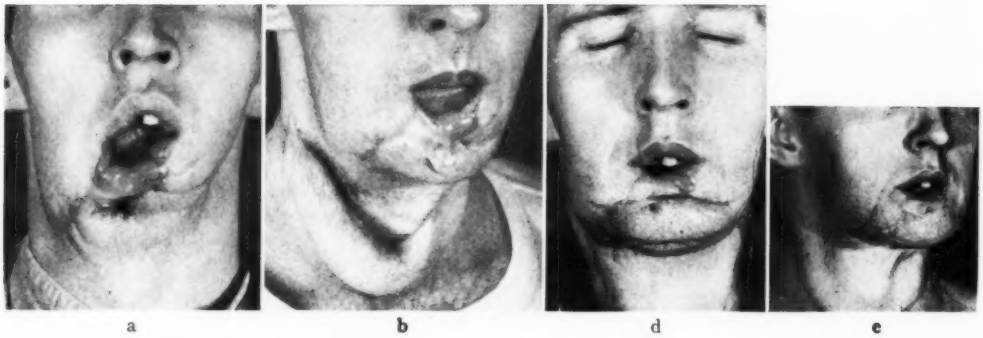

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Fig. 5. J. L., Pvt., aged 22 years, received a shell fragment wound of the face October 19, 1944, with avulsion of soft tissues of the chin and loss of the symphysis and anterior two-thirds of each body of the mandible. a, Appearance on admission. b, Pedicle flap raised from chest to allow for shifting of neck flap upward into defect. c, Roentgenogram showing block grafts in tantalum tray. d, Appearance following operation showing contour of the mandible. Note pedicle tissue has been smoothed out on neck. e, Final appearance following rearrangement of soft tissues of chin.

minimizing bleeding in the operative field. In addition, the patient is less likely to develop postoperative respiratory distress and nausea when a general anesthesia can be avoided.

TECHNIQUE

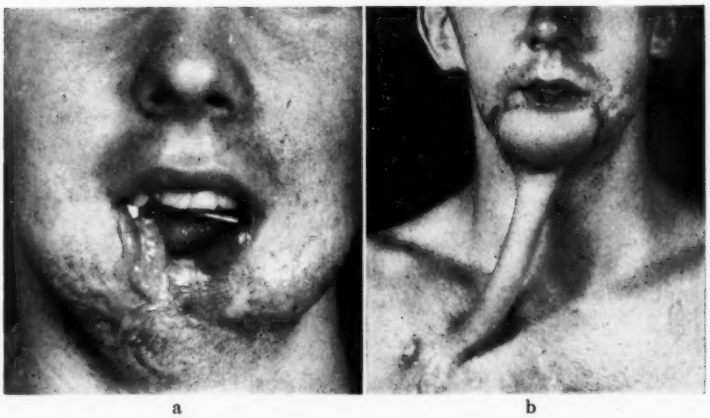
The operative technique is as follows:

Incision is made parallel to the lower border of the mandible with care taken to prevent injury to the mandibular branch of the facial nerve. This nerve can be avoided by dissection downward external to the platysma for about 2 centimeters below the inferior border before approach is made to the bone fragments. About 2 centimeters of bone is exposed on each side where fragments contain teeth. For ramus, angle, or posterior edentulous fragments, exposure can be made by stripping the periosteum for long distances without danger of entering the oral cavity. Edentulous fragments are detached thoroughly and replaced in normal position.

Eburnated ends of fragments are cut off by sharp rongeurs, and the outer cortex of the mandible in the recipient areas is removed with a dental burr until an area of bleeding bone sufficient for good contact is obtained.

Meanwhile the iliac crest has been exposed subperiosteally by another operative team. A large section of ilium is cut out with a sharp osteotome and placed on a wooden block for removal of all cortical bone, which is then discarded. The donor area is closed in layers with a deep removable No. 32 wire suture, and No. 36 interrupted sutures are used for the skin. Pressure dressing is applied.

The graft is shaped with sharp-cutting rongeurs, and all cancellous chips are saved to be packed later into open spaces in the graft bed. The transplant is placed in position as both an inlay and onlay graft and is immobilized by a single strand of No. 32 stainless steel wire at each end. At least 2 centimeters should be in contact with the bleeding bone on each fragment. Although there may be marked protuberance externally at first, rapid absorption takes place, and the contour of the mandible is quickly established after function begins



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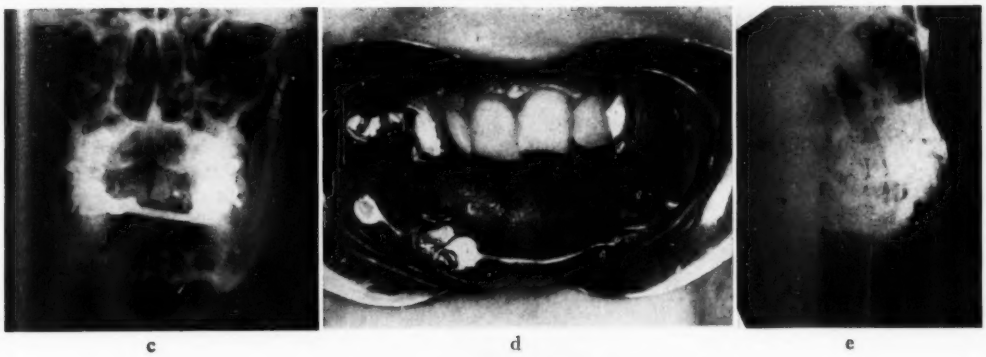

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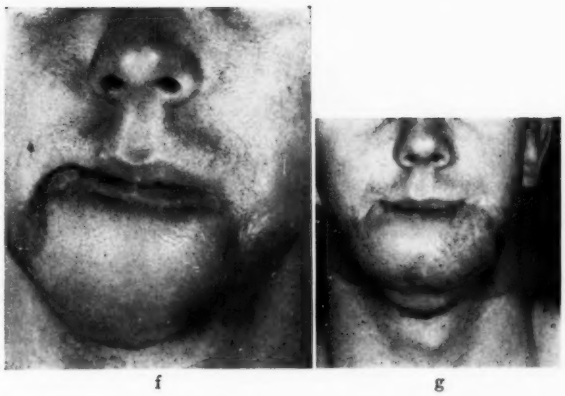

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Fig. 6. F. W. P., Pvt., aged 20 years, received a shell fragment wound July 7, 1944, with avulsion of the lower lip, chin, and floor of the mouth, and loss of the symphysis and anterior one-third of each body of the mandible. a, Appearance 3 months after injury. b, Pedicle flap in position. c, Roentgenogram showing bone loss. d, Interlocking cap metal splint used for immobilization of fragments before bone grafting. e, Roentgenogram showing bone graft in position. f, Appearance following firm bony union. g, Appearance following excision of outer covering of flap and replacement with skin from the face. Further "touching-up" procedures are yet to be carried out.

Complete hemostasis is obtained by ligation of all bleeding points with No. 40 wire. Closure is made in layers, and firm pressure dressing is applied. It cannot be too strongly emphasized that there must be no tension on the wound edges, and it may be necessary for proper relaxation of the tissues to undermine the skin for considerable distance.

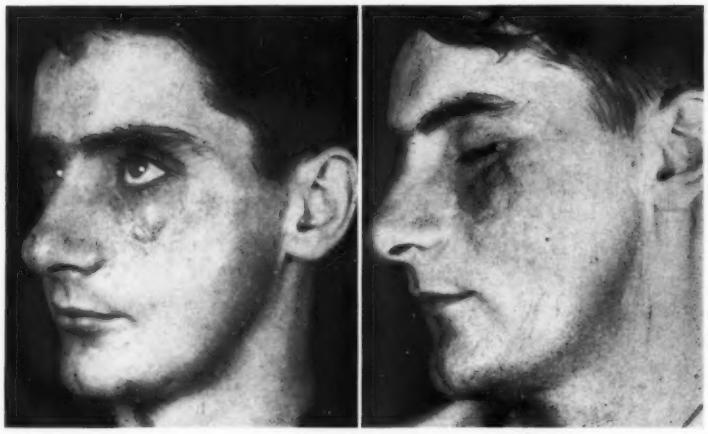

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Fig. 7. J. P. P., Pvt., aged 19 years, received a shell fragment wound of the face June 24, 1944, with fracture of the left mandible and maxilla. Following removal of an unsuccessful cartilage graft because of drainage, a large cancellous bone graft was placed over the remaining portion of the maxilla, with good contour resulting. a, Appearance on admission. b, Final contour.

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a b

Fig. 8. C. C. Pfc., aged 19 years, received a shell fragment wound of the face July 15, 1944, with avulsion of soft tissue and loss of the major portion of the left maxilla. The soft tissue loss was replaced by pedicle skin prior to restoration of contour by a cancellous block graft. a, Appearance on admission. b, Appearance following operation. It is planned to remove the outer covering of the pedicle flap as completely as possible at a later date and replace it with a rotational flap from the neck.

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In over half of our cases closure was made with fine silk, but as we felt that in two instances drainage occurred as a result of buried silk sutures, we began to use a single removable stainless No. 36 wire for the deeper layers and continuous running stitch of No. 38 wire for the skin.

AFTER-CARE

Postoperatively patients are kept in a semisitting position and watched closely for evidence of respiratory difficulty. In one instance we found it necessary to open an intraoral splint for 24 hours to relieve obstruction. Liquids are given by syringe or tube, and gradually the patients learn to put semisolid foods around the splints with the fingers. Protein and vitamin intake is given careful attention.

Routinely we have given for 5 days postoperatively 20,000 units of penicillin in ¼ per cent novocain solution every 3 hours. Pressure dressings to both donor area and face are maintained for 10 days, and frequent mouth wash is used for oral hygiene. Patients are usually ambulatory by the end of 2 weeks. After 7 or 8 weeks the cap metal splints are released, and the state of clinical union is inspected. If the fragments are not absolutely rigid, splints are left in place for another 2 to 4 weeks before removal. Dentures are fitted within 8 to 14 weeks if normal buccal and labioalveolar sulci are present. Otherwise these must be reconstructed by stent grafts 4 to 6 months later.

During the past 2½ years we have seen in an army plastic surgery center 68 patients who have required bone grafting because of mandibular loss greater than 2 centimeters. Eight of these showed massive avulsion wounds which required replacement of soft structures by pedicle flaps prior to bone grafting. Two of the 68 patients are still waiting final operation pending subsidence of tissue reaction.

In the remaining 66 cases blocks of pure cancellous bone from the ilium have been employed for defects varying from 3 to 15 centimeters in length. Drainage has occurred in 10 instances: twice from buried silk; three times from inadequate coverage; and in 5 cases from accidental opening into the oral cavity. Half of these cases have had successful union in spite of drainage. Four have had partial loss of graft; 2 of these have since been regrafted without complication. In the fifth case it was necessary to remove the transplant because of infection. Failure has been attributed in 3 instances to insufficient cover plus difficulty in fixation for one reason or another; in 2 there had been infection following entrance into the mouth.

No disability has been noted in any patient from the removal of bone from the ilium. Drainage has occurred in 2 instances, once from buried silk and once from a small piece of rubber tissue inadvertently left in the wound.

In addition to 68 bone grafting procedures to the mandible in 66 patients, cancellous iliac grafts have been employed for restoration of contour in 18 deformities of the maxilla, 5 of the nose, and 2 of the supraorbital margin. Drainage occurred in one instance, but successful final union was obtained in every one of these cases.

SUMMARY

In summary, we believe that iliac block grafts of pure cancellous bone form the most satisfactory material for relief of large and small bony defects in the mandible. The large percentage of cases without failure cannot be attributed to the choice of graft alone, however. We must not overlook the value of chemotherapy in the treatment and prevention of infection nor disregard the importance of suitable mechanical fixation of fragments. Above all, we must not forget that the background of all transplantation procedures is the proper preparation of the tissues themselves. In no other branch of surgery is the old adage so true, that "haste makes waste."

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MODERN METHODS IN THE TREATMENT OF FRACTURES

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IN the early days of the human race, nearly all fractures were caused by falling from a sufficient height, and were usually simple fractures of the long bones. As the centuries rolled by, and warfare became developed to a higher grade than wooden clubs and stone axes, compound fractures became more common and were less easily repaired. With the advent of gunpowder and the hazards of more rapid transportation, fractures occurred with much greater frequency, and began to attract the serious consideration of the physicians and surgeons of those times.

Seventy years ago, a compound fracture of an arm or leg almost invariably required immediate amputation to save the patient's life, but the development of antiseptic and aseptic methods of treatment began to offer more hope of saving these damaged limbs. Forty years ago, the rapidly increasing numbers of automobiles introduced the tremendous risks of high-speed travel on the highways and the byways of the world. Thirty years ago, the first World War produced the enormous dangers of high explosives and fast airplanes, and these dangers were multiplied many times over in the war which ended only last year. Or has it really ended?

What has been learned in the last few decades about the treatment of fractures? Since 1900, forty-six years ago, I have been interested in orthopedic surgery and in fractures. I have seen the rise, and sometimes the fall, of many different methods and ideas in the treatment of broken bones.

The one dominant purpose of treatment is to produce a satisfactory union of the fracture, with re-establishment of the normal function, in the shortest possible time.

In the Fracture Oration of 1935, Paul Magnuson presented briefly and graphically the salient points of fracture treatment from the days of the Egyptians 4500 years ago, the Hippocratic era 2400 years ago, and the works of Galen up to the year 200 Anno Domini. Then came the long centuries of the Dark Ages when no progress was recorded until the Renaissance. In the 14th century, interest in fractures was revived, and from that time the value of many of the almost forgotten old principles began to be recognized. Methods of traction and countertraction, the basic foundation of the treatment of fractures of the long bones, became simplified and improved. Buck's extension, Thomas's splint (which was originally designed for knee disorders) and the Hodgen suspension splint gradually assumed their well deserved importance, together with the improved types of adhesive plaster. Then, in 1895, came Roentgen's discovery of the x-ray, which visualized both the good and the bad results of treatment, and made possible some much needed improvements in the handling of fractures.

Now it became easy to determine accurately whether or not the alinement of a fractured femur was satisfactory, or whether the traction was pulling the bones too far apart.

Next came the development of skeletal traction by Steinmann's pin and Kirschner's wire, in cases in which adhesive plaster could not be used. These devices were not free from the danger of infection and had to be carefully watched.

In 1910 Arbuthnot Lane popularized his method of applying a steel plate, by open operation, screwing it across the fracture-line by four or six or eight screws. This simple and easy way of reducing and securing fractures of the long bones swept the country like a tornado. It seemed so rational and so satisfactory that hundreds of surgeons purchased the plates and the few special instruments, and, without following the meticulous technique perfected by the originator, proceeded to plate many simple fractures of the long bones. I do not know how many times I have been asked

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to see a boy or a girl with a fractured femur who was about to have a Lane plate applied by an enthusiastic surgeon. In most of these cases, when it was explained that the overriding and the malposition could be corrected by a few days of traction and suspension in a comfortable Thomas splint, and that in 6 or 8 weeks union would be strong enough for a caliper splint or a plaster-of-Paris spica, the doctor and the patient were willing to avoid the operation.

There are two basic reasons, entirely apart from the danger of infection, why a plate of the Lane type, or the Sherman type, or any similar type is not the ideal method of treatment. First, it does not immobilize the fracture completely, because a certain small amount of motion will always be present in rotation and in lateral bending toward the plate. Both of these motions could be avoided by applying a similar plate to the opposite side of the bone, but few surgeons have had the hardihood to attack the bone on both sides. In oblique fractures, a transfixion screw applied at right angles to the line of fracture will prevent most of the mobility, but does not work so well in transverse fractures. Secondly, when a Lane plate is applied, the ends of the fragments undergo a small amount of absorption, so that a definite space is left between the ends. It is true that in many cases enough new bone is formed to obliterate this empty space, and the fracture unites, but it does not unite as rapidly as it would if the bone ends were in firm contact. Moreover, the external callus formation develops upon the opposite side of the fracture, and does not cover the plate, except in children, so that the ultimate ossification of the fibrous tissue between the ends of the bones is greatly delayed. This external callus may become very large when the immobilization of the fracture is inadequate. Even a long plaster-of-Paris cast, from the chest to the toes, does not furnish complete immobilization in most cases of fracture of the shaft of the femur.

I do not deny that in many hospitals and clinics the plating of simple fractures of the long bones has shown excellent results, but such operations should be performed only when a satisfactory result cannot be obtained by conservative mechanical means, and when the surgical standards of the operator and of the hospital are of the very highest grade.

Because of the many disappointments following the widespread use of the early types of the Lane plates, whether from mechanical defects, technical errors, or infections, other investigators have been busily devising different methods. The old and reliable principles of manual reposition, traction, and countertraction, and fixation by plaster of Paris and splints have become less understood and less popular. This, I think, is largely due to the fact that the conservative, mechanical treatment of long bone fractures requires the careful, time consuming attention of the surgeon himself. He cannot safely delegate this attention to anyone else. A leg or an arm in a traction apparatus must be seen every day by the man who is responsible for the ultimate result. Residents and internes do not always notice that the adhesive plaster is cutting into the skin or is losing its pull at important points. Because this constant attention is necessary, and because a day has only so many hours, it is perfectly natural that busy surgeons should welcome any methods which would reduce the time element required for proper results. If such methods are safe, sane and satisfactory, we should use them, but we must always remember that the union of a fracture takes so many weeks or so many months, and that we cannot make broken bones grow together any faster in 1946 than the Egyptians could four thousand years ago.

What are some of these newer methods, and to what extent can they be recommended for general use?

Many years ago various types of nails and screws were employed in attempts to fasten together the broken bones. Considerable success resulted, in many cases, but the ever-present danger of infection made such treatment always a definite hazard. The advent of the sulfa drugs, penicillin and other fungus derivatives has removed some of these dangers, but there is still no substitute for aseptic surgical technique. Stainless steel and vitallium have replaced iron and plain steel, and we can no longer use metals which undergo erosion or cause electrolytic reactions in the

body tissues. Metallic fixation of fractures has assumed a very important place in bone surgery, especially in certain kinds of fractures. The neck of the femur, the olecranon process of the ulna, the patella, and the shaft of the tibia may present problems which may legitimately be considered suitable for open operation. Years ago, Kellogg Speed, in one of these Fracture Orations, applied the name "The Unsolved Fracture" to the very dangerous fracture of the neck of the femur. The medical literature has been full of articles about different methods and devices for the treatment of this lesion. When I was a young man, some of the surgeons were using carpenter's screws or nails, with occasional success but with frequent failure. Smith-Petersen's three-flanged nail was an enormous improvement over the earlier types, but even today there are clinics where lag-screws, threaded wires, and other devices are preferred to the flanged nail.

Some of the recent publications do not emphasize sufficiently the enormous necessity of accurate reduction of the fracture before it is nailed or screwed. In many of the articles, roentgenograms are shown which reveal imperfect replacement of the fracture before the nail was inserted. This did not always produce a failure of union, but it is certainly not desirable, and it is usually the result of inadequate x-ray control. Anteroposterior x-ray films cannot be relied upon to show accurate reduction of the fractured ends, and it is extremely difficult to make satisfactory lateral films with the patient's legs fixed firmly in the traction apparatus. No surgeon should attempt to nail a fracture of the neck of the femur unless he can obtain good lateral films on the operating table at all stages of the operation, without disturbing the hip-joint or the operative technique. This means that such patients should be cared for in a hospital with all of the requisite equipment and personnel. It is major surgery of the most difficult type.

The purpose of this lengthy discussion is to emphasize the tremendous importance of developing, in every community, a team of surgeons who will be able to treat properly the cases of fracture of the neck of the femur, and who will have the requisite instruments and x-ray facilities and technicians, without which no one can accurately reduce and nail such fractures. One day in August I examined the x-ray films of 3 cases of this kind which had been nailed in other cities. Not one of these fractures had been properly reduced before the nailing, and all 3 had failed to unite. It is highly probable that these unfortunate results were due to imperfect lateral x-ray films made on the operating table, and I have seen many similar examples, 2 of them occurring in my own practice. Unless the x-ray control is clear and accurate, it will be necessary to open the hip-joint in order to be sure that the reduction is satisfactory and that the nail is put in the proper place. This type of open operation adds greatly to the danger of shock and of infection, and is practically never necessary when good x-ray films are available during the operative procedures.

To make my position perfectly clear, the following plan seems to be the best for the treatment of fractures of the neck of the femur:

The patient is placed upon an orthopedic traction table of the Albee, Hawley, McKenna, or similar type. The displacement is carefully reduced by the Leadbetter maneuver or by traction. X-ray films are made in anteroposterior and lateral planes, one of the two portable tubes being located between the thighs, the other directly over the hip-joint and two or three feet above the field of operation. The perineal post on the sacral support should be of wood or aluminum, so that no manipulation will be necessary for the lateral views. When the reduction is shown to be satisfactory, both legs are securely fastened to the traction apparatus. A 5 inch incision is now made to expose the outer surface of the femur, and a long wire, marked in half inches, is drilled upward and inward from a point well below the trochanter. It is wise to make a hole through the outer cortex with a quarter-inch drill before starting the wire, so that the direction of the wire can more easily be changed without binding or bending in the thick cortex. When the wire has been inserted to a depth of 3 or 3½ inches, new x-ray films are made to check its position. If not satisfactory, the wire is withdrawn and reinserted until it is

in proper position. This may require one or two trials, with corresponding x-ray films. A little time may be saved by using another wire, leaving the first in place as a guide. When the position is found to be correct, a cannulated stainless steel or vitallium Smith-Petersen nail is threaded upon the wire and is driven along it into the neck and head of the femur. The length of the nail is estimated by the calibrations of the wire. Again, x-ray films are made in both directions, and, if satisfactory, the wire is pulled out and the wound closed.

You will see, from this description, the enormous importance of the x-ray examinations, and the complete futility of attempting this kind of operation unless such rapid and accurate roentgenographic control can be furnished. Good anteroposterior views can be made with great ease, but the lateral views require special equipment and technique.

I have not mentioned the use of screws, lag-screws, or the various threaded or unthreaded wires, because I believe that the Smith-Petersen-Johansson nail is better than any of them for general use.

A few words about the after-treatment. Over the usual dressings a firm, elastic spica bandage should be applied from the waist to the knee, and a foot-piece or sling should be used to prevent outward rotation of the thigh.

It is important to prevent outward rotation of the thigh as the patient lies in bed, because the weight of the thigh and leg exert a downward and outward pull upon the nail, tending to separate the fragments. It is not wise to allow early sitting and standing without some form of partial immobilization of the affected hip, although some writers encourage it.

We must remember that at least 4 months are required for bony union in these cases, and that union is made by the internal deposit of new bone, and not by external callus formation.

Aseptic or avascular necrosis of the femoral head is a complication of intracapsular fractures seen less frequently than after dislocations of the hip, but nevertheless sufficiently often to influence the ultimate prognosis. The artery in the ligamentum teres supplies only a small portion of the head, and, indeed, is sometimes absent. The main blood supply comes from the arteries of the capsule, and if these arteries are occluded or are too small, the head becomes necrotic. At present, there is no certain means of improving the blood supply, although drilling and bone-grafts offer some hope. Perhaps the best form of treatment is to prevent any weight-bearing on the femoral head, by the use of crutches and a caliper splint, or by long-continued traction, trusting that Nature will provide a new blood supply by the slow ingrowth of small arterioles and by "creeping substitution." This requires a long time, and in some cases fails to occur, in which event the patient has a painful and disabled hip-joint which may need a reconstruction operation, or an arthrodesis to produce an ankylosis of the joint.

Let us now consider the other types of fractures which may usually be considered suitable for operative treatment. The patella and the olecranon process of the ulna, if the fragments are widely separated, will unite more satisfactorily and more rapidly if they are mechanically fastened together by one of the accepted operative methods. Spiral or oblique fractures of the shaft of the tibia may be extremely difficult to retain in good position by conservative treatment, and it may be wise, in such cases, to fix the fragments together by transfixion screws, or even by stainless steel plates. The fibula unites much more rapidly than does the tibia, and sometimes holds the fractured surfaces of the tibia so far apart that they cannot unite. Cases of this kind require operation.

For many years, the surgical literature has been flooded with articles advocating the use of mechanical devices for the reduction and the fixation of fractures of the long bones. The catalogues of the instrument-makers and the published articles of the designers show in fascinating detail the very ingenious devices and the remarkably successful results. The basic principle of all of these contrivances is identical. This principle is to drill two strong pins into the shaft of the bone above the fracture and two more similar pins below the fracture, as far away from the fracture itself as possible, and to connect each pair of pins with a clamp to hold them rigidly to-

gether. These two units are then used to manipulate the fractured ends into accurate apposition. In difficult cases an ingenious traction frame has been devised to aid in this manipulation. When good position has been attained, the pin units are connected by rods clamped firmly to them, or by short plaster-of-Paris casts molded around the pins. It is not to be denied that this method is very valuable in certain types of fractures. It furnishes good apposition and good control of nearly all types of fractures, and allows early and free movement of the joints at either end of the broken bone. It is, however, neither so simple nor so safe as the inventors and manufacturers would have us believe. It requires considerable skill and experience to drill the pins into the proper positions, whether the pins go entirely through the limb, or stop after penetrating both cortices of the bone and project only from one side of the limb. It is also not easy to prevent infection from occurring along the track of the pins, as there is always some seeping discharge from the pin holes, but the advocates of the method state that osteomyelitis is very rare.

The best known of these devices are the Stader, the Haynes, the Griswold, and the Roger Anderson types, and of these the Anderson instruments seem to be the most generally satisfactory. They are all modifications and improvements of the old Lambotte ideas, and in a very small proportion of fractures they may be very useful.

Another revival of ancient methods was described by Kuntscher in 1940, who drove a long steel rod into one end of a fractured long bone, down through the medullary canal across the line of fracture. These rods were used chiefly in Germany during the second World War, and have achieved some popularity in the United States. One of the advantages of this method is that the broken ends of the bone are pulled into close apposition by the action of the muscles, so that union is much more rapid than when Lane plates are used. The fact that the medullary canal is plugged up by the rod seems to have no deterrent effect upon the union of the fracture.

About thirty years ago Hey Groves treated a fracture of the upper third of the femur in this way, using an iron rod, but he complained that the rod was not strong enough to resist the muscle-pull, and so the femur became bent at an angle. If he had put the leg up in a Thomas splint or in plain traction apparatus, after the operation, the result might have been better. With the new stainless steels, the method may be useful in selected cases.

It must be admitted, in discussing the various kinds of operative treatment of simple fractures, that the advent of the sulfa drugs and the fungus derivatives has made open surgery much safer than it was a few years ago, but we must not lose sight of the fact that the majority of fractures can be treated successfully by the older conservative methods. We are going through a transitional period at the present time, both surgically and politically, and I do not want our young physicians impressed with the idea that fracture treatment necessarily means a machine-shop full of tools to repair every kind of broken bone.

The best fracture surgeon uses the fewest gadgets.

THE SURGEON AND HIS TRUST

With Special Reference to Safe Conduct of the Patient through Operation

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THE safe conduct of a patient through operation demands the following: (1) adequate preparation of the surgeon, (2) careful and precise preparation of the dissection, (3) satisfactory preparation of the patient for, and adequate care of the patient after, operation. All of these items are important. Inasmuch as many of the important items relating to care of the patient before and after operation, the subject of this symposial discussion, have been dealt with in an eminently satisfactory manner by the other participants, I have elected to devote my remarks principally to a somewhat philosophic consideration of the surgeon's own preparation for his responsible tasks. I do not interpret my opportunity of speaking last as affording me the privilege of acting as moderator in this discussion. In the final analysis, you and time are the ultimate arbiters and umpires of what is said here.

THE FUNCTIONS OF SURGERY

The very nature of surgery stamps it as a sacred trust. By general agreement, surgery is invoked only when the desired objective cannot be achieved satisfactorily by nonsurgical means. It is the purpose of surgery to preserve life and to restore normal function in so far as is possible, and at the least risk to life, and without compromise of the patient's future welfare.

FORMALITIES OF SURGERY

Any enterprise which achieves its ends through employment of such extreme means as surgery must of necessity observe certain formalities. In saying this, I am not alluding to fatuous conventions and empty ceremonies but to compliance with rules of conduct which time and practice have shown to be valuable guides.

The items listed above which have to do with the safe conduct of a patient through operation are mutually interdependent. One component is unlikely to afford promise of success without the co-operation of the others. A well trained surgeon who comes well prepared for the operation and who performs a superb dissection but who neglects the preparation of his patient before operation or his care after operation is not doing the best for his patient, and the surgeon who bungles the dissection stands in the way of recovery of his patient. Yes, poor preparation of the dissection is alas the agency through which some patients who undergo surgery with the hope of having their lives made happier and longer have them shortened. How poor management of the problem of hemostasis in any type of surgery but particularly in operations involving large blood vessels; or performance of an anastomosis in the gastrointestinal canal which is architecturally unsound may shorten the lives of patients needs no elaboration. What surgeon would not prize highly an opportunity to be given a second chance to rectify an error of commission which shortened a patient's life? But an operation like any biological experiment is performed only once. Why not prepare well for it? Death is so final!

Yet, we see surgeons hurrying through operations, as though their time were more important than the safety of the patient. Has not the fallacy of the "get in quick and out quicker" approach to surgical problems been exposed sufficiently? No amount of best care before and after operation can undo the harm of an operation badly performed.

Wise surgical planning limits the surgeon's range of activity. The Army Medical Corps in World War II had a record of accomplishment in the management of difficult surgical problems which was unique in the annals of medi-

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cine. The success of that undertaking was the result of planning, organization, and the selection of individuals with satisfactory training to do a given job. In our own work, we are left largely to our own devices in these matters. The product of our endeavors is dependent in large measure upon how well we have planned and the care with which organizational detail has been carried out. The range of operations which any one surgeon may perform is also a matter of personal choice. This latter item is a matter which demands some standardization among surgeons, just as much as particulars of planning and organization. There are still a few surgeons who affect to believe that they can take all of surgery for their province. They know as well as anyone that their performance in such a wide category of operative procedure is substandard in some of these areas, when judged in the critical light of what constitutes good practice. If a surgeon has not the moral courage to say to himself occasionally: "The interests of this patient are served better by having someone more intimately acquainted with the problem undertake this task than I," when will society or medicine set up an advisory group with authority to decide for us that which we have been unable to decide for ourselves?

Even among teachers of surgery who have a better opportunity for continued self-improvement than the rank and file of surgeons, there are still a few who essay to embrace a large portion of all of surgery. In our time, we have seen the province of the general surgeon shrink; so much so, that occasionally we wonder what areas of surgery are embraced in the designation general surgery. Yet, this is as it should be. If a teacher of surgery were so ardent a student of his art that he wished to encompass the entire field, an aspiration more ambitious than praiseworthy, he would remain all his days a learner and would thereby lose the important opportunity to give directional growth to a smaller sphere of surgery. Teachers of surgery must prove themselves in the next generation as well as in this. The teacher who leaves no pupils or intellectual progeny has not been fully alive to his responsibilities or wholly faithful to his trust

The passing of the all-around surgical specialist. The sprouting of many surgical specialties from the parent stem of general surgery affords some indication of how surgery has grown. Moreover, sharper lines of distinction between the various surgical specialties are being drawn. The specialty boards are playing an important rôle in lending acceleration to this transition. In some clinics not so long ago one could see a surgeon, in a single day's work, do a stomach operation or two, a few operations upon the biliary tract, as well as the colon and rectum, and perhaps a few goiters and a breast operation or two in addition; and then extend himself into the province of the urologist, gynecologist, and orthopedist. Let us be thankful that the day of the all-around surgical specialist is done! Surgery is not advanced by that type of activity and no matter how talented the surgeon he cannot do equally as good work in all these provinces.

The background of training of the surgeon should be broad. But having acquired orientation and competence, a surgeon must of necessity, if he aspires to rise above mediocrity, give selective direction to his activity instead of trying to grow in all directions simultaneously. The public has the right to demand a high standard of performance from us. Moreover, we are all debtors to our profession and from those of us who have enjoyed opportunities above the ordinary, society reasonably may expect that we should strive to add something to the sum total of knowledge rather than continue to be parasites upon our common heritage.

The responsibility of higher institutions of learning to surgery. Surgery has been enriched from many sources. Our institutions of higher learning have a responsibility for leadership in surgical education in this country—not alone to train students for the practice of surgery and to help them meet the requirements of the Specialty Boards, but also for the great task of improving surgery. Recognition of the tremendous importance of research in lending accelerated momentum to the slow growth of knowledge is a part of that responsibility. Knowledge can come to have new meaning with synthesis of well known

facts and much of surgery's progress in the past decade has been compounded out of well known facts becoming known to the right persons. It is to the discovery of new fact, however, that we look hopefully to the future for significant changes and improvements in surgery that will have the same impact upon our lives as did the discovery of anesthesia and asepsis.

The acquisition of surgical techniques. The acquisition of skills is an interesting study. Those of us who have been privileged to be teachers of surgery and who have nurtured young "surgical plants" have had a unique opportunity to observe how such "seedlings" grow. Given a good brand of "plant" with a high native intelligence, and a real capacity for application, accompanied by an intense and unflagging interest in surgery together with a sympathetic understanding of the frailities of man, the capacity for growth of such an individual is almost limitless. And, if in addition he is possessed of an inextinguishable yearning to add his bit, whether large or small, to the sum total of surgical knowledge, there is no telling how far he may go. That he will surpass his teacher in accomplishment is self-evident. There is a certain inertia or lag in the learning process when progress is made slowly if not almost imperceptibly. But all of a sudden the man who just yesterday seemed almost a novice becomes an accomplished technical surgeon. The circumstances which bring about this accelerated spurt of growth are difficult of assessment and are not readily defined. It is not a process that can be hurried but a development which must come naturally through a certain sequence of events, which by no means is the same for all individuals. This development has to do with the surgical neophyte becoming steeped in the practices, techniques, and procedures as well as the general approach of a surgical service to problems. In this learning process, acquaintance and an increasing familiarity with the numerous facets of individual surgical problems, as they relate themselves to physiology, biochemistry, or bacteriology, are very important. This period of training constitutes essentially an apprenticeship. For the finished surgeon, it is a *sine qua non*. The surgeon who is self taught is distinguished readily from the person who has pursued this more rigorous and orthodox scheme of training. And, how quickly the surgeon of ability, who has traveled this devious and stony path, learns to master the technical phases of difficult operations is always a source of amazement and gratification to me. It is a metamorphosis in which the co-ordination of eye, mind, and hand are important. The man who can grasp the problem and transmit to his hand what the eye sees and exact from this eye to mind to hand relationship a high standard of performance—that man is the superior surgeon. Before this co-ordination is effected the surgeon seemed but a fledgling, but when that time comes almost overnight he becomes an accomplished surgeon whose work reflects confidence in his own performance. Only the surgeon who has trod this steep and winding path can know the cost! Is it worth the effort? Ask any of these men and examine the product critically! Truly, there is no royal road to learning.

This circumstance of how quickly the trained surgeon masters operative techniques augurs well for the future of surgery. It suggests how we see further than our predecessors because we stand on their shoulders; in turn, our students stand on ours. It is a promising prospect for surgery, the continued growth of which is assured in the hands of the present keen generation of surgeons who are beginning to make their mark. As Leonardo da Vinci remarked, "It is a poor pupil who does not surpass his master."

Motivation of the surgeon. One need not gossip long, in the medical sewing-circle, the confessional in which the sins of our neighbors are confessed more adequately than one's own, to learn that surgeons are not generally held in that high esteem by our medical colleagues to which we would aspire. There are those who look upon the surgeon as a manual laborer in a Greek dress. There are even those in our own midst who affect to believe there is less science than art in surgery. And many of our medical colleagues, who are not as accustomed or as adept as we in employing their hands in the service of their brains, are bold to suggest that surgery is only a trade, para-

sitic upon the generous gifts of medicine. Take away the petty skills from most surgeons, they say, and see what empty sacks remain. Are these critics unmindful of the tremendous impetus given greater medicine by the discovery of anesthesia and antisepsis? Have they forgotten how the ministrations of the surgeon make an important contribution to the daily enjoyment of, and in many instances to the extension of life?

It seems to me that trained surgeons schooled in the scientific method hold in their hands important tools by which to push back the boundaries of medical ignorance. A disciplined imagination lies at the bottom of every great discovery. The most important requisite of any promising research project is an idea. Surgeons who aspire to make contributions to the patrimony of knowledge would do well to school themselves in the techniques of one of the biological sciences, such as bacteriology, biochemistry, or physiology. I hold strongly to the belief that for the surgeon who aspires to a career in academic surgery that 2 years spent in acquiring the technique of one of these provinces of knowledge will pay usurious dividends not alone to the individual but to surgery and greater medicine as well.

The author of a recent thought-provoking and deservedly popular book[1] writes, "The surgeon's skill sometimes is a splendid example of the sublimation of an early childhood urge to cut." A well known psychiatrist[2] wrote a few years back, "Leaving aside all secondary conscious motives for operating other than those provided by reality, we realize that much surgery betrays evidences of being undisguised sadism." I resent such implied or expressed innuendos concerning the motivations of the surgeon. I associate daily with surgeons who give no evidence of such sadistic repressions. If the truth were known, the reasons generally are probably far simpler and find their likely explanation in why men become grocers, lawyers, or engineers. You see before you a boy, grown to manhood, whose consuming ambition was to continue his activities on the farm that he loved so much. His discerning father suggested that ministering to the physical ills of man would prove even more satisfying than lavishing care on cows, horses and pigs. This was difficult for a growing farm boy to believe. Inasmuch as the spirit of compromise resolves most differences, I suggested veterinary medicine as a substitute. My father far wiser than I continued to insist that medicine was a better outlet, and so I came rather unwillingly into medicine and surgery, pushed in through the back door. "Contented industry," said the late Wm. J. Mayo, "is the mainspring of human happiness." And when that labor has to do with making the lot of man more endurable, what employment could give greater happiness? I feel certain that the services of a psychoanalyst need not be enlisted to ferret out the compelling reasons that urged many of you to become surgeons.

It is, however, probably not out of place to suggest that envy, because of the relatively larger incomes earned by surgeons and especially by surgical specialists, lies at the root of much of the criticism directed at surgeons by their medical colleagues. On this score I shall only say that, for the years that lie ahead, surgeons and other medical specialists paid out of proportion to their contributions to the advancement of medical knowledge, as judged from the critical viewpoint of the true scientist, would do well to consider receiving part of their emolument as increased opportunity. Society rewards us generously for our responsible labors in the relief of suffering and the betterment of man's lot. If, however, we value even more the approbation of our colleagues with scientific leanings—a consideration which is not unimportant—some thought might well be lent to utilizing partially the potential earning capacity of surgeons as well as that of other highly paid medical specialists to afford ourselves better conditions of work, thereby improving the product of our labors, and at the same time lending a helpful stimulus to surgery. No doubt, many of you already have resolved this problem in some such manner. Satisfactory conditions of work and an opportunity for creative effort are valued by the thoughtful surgeon as among the best

[1]J.L. Liebman. Peace of Mind, p. 28. New York: Simon Schuster, 1946.
[2]Karl Menninger. Psychoanal. Quart., 1934, 3: 173.

of paymasters. No one fears that the successful surgeon will starve! The tissues of the rich and the poor patient present the same problem to the surgeon. And the inarticulate but touching gratitude of a patient, who cannot pay in the coin of our realm, is nonetheless among the best of all rewards of the surgeon.

The surgeon and particularly the older surgeon will do well to contemplate occasionally his motivations and incentives and revalue anew his rewards. Let him also reaffirm periodically the Hippocratic Oath! When long years ago this writer was confirmed in the faith of his fathers, the preacher employed on the occasion a text from the prophet Jeremiah: "Stand ye in the ways, and see, and ask for the old paths, where is the good way, and walk therein, and ye shall find rest for your souls" an instruction equally as important for surgeons as well as for Sunday school communicants. Can there be greater rewards than the satisfaction and the peace of mind which come from having served his fellow man well? Our yoke of duty and responsibility may be heavy but whose opportunity and privilege to bring happiness to others is greater?

The Federated Surgical Society of America. The Regents of the American College of Surgeons previsioned the avid curiosity and thirst for new found knowledge on the part of the practising surgeon, when they instituted the Forum on Fundamental Surgical Problems. The continued interest in this type of program by the general surgeon in practice affords ample demonstration of the wisdom of that decision. And as more of America's best young surgeons who went to war return and manifest renewed zeal to contribute to the advancement of surgical knowledge, an even more critical selection of papers for presentation can be assured. The time is now ripe for the formation of the Federated Surgical Society of America embracing all the ancillary surgical specialties, much in the manner of the Federated Biological Societies in the preclinical divisions of medicine. That society serves medicine in a unique manner. A similar organization of surgery and its various surgical specialties employing the prototype of the Surgical Forum as its pattern would lend renewed emphasis to the importance of research in surgery. At the same time, it would constitute an important agency in giving better integration to the many, now somewhat distinct, branches of surgery. Is not the American College of Surgeons the parent society which should foster this development?

Have surgical meetings had any influence on your intellectual growth and development? They have on mine. Man cannot lift himself up by his bootstraps; neither can surgical societies increase surgical knowledge save in so far as they encourage an interchange of ideas between surgeons at the best possible level. Surgical specialists in the same field are not long the best company for one another. There is not enough stimulating sustenance in that type of association for continued growth and development, no matter how interesting the interlude provided by such exchanges. The life-giving spirit and vitalizing influence derived from close association with fellow colleagues in the broad domain of medicine is indispensable for the surgeon.

Surgery is on the move. We respect the traditions of the past, but the empiricism of surgeons of generations just past is being displaced by the appreciation of and more frequent employment of the scientific method. The touchstone of the scientific method lies in the universal validity of its results. It affords a finality which sets aside all room for continued speculative rationalization. While we are debating and airing our respective opinions on a controversial subject, some enterprising individual constructs and carries out the crucial experiment which reveals the truth in the matter. How sterile and unprofitable are discussions based solely on impressions, no matter who the authority. Not even the experienced investigator makes a "ten-strike" each time he sets up an experiment. No, the progress of research is slow. Yet, fact correlated with fact builds a structure which will stand against the winds of time.

It is from the lips of men who are engaged in the exciting pursuit of fact finding that, we may expect that stimulating refreshment which makes us better surgeons for the experience. The acquisition of knowledge is not a passive process. Listening to the recital of the train of events which led up to an im-

portant discovery does not make us better surgeons. It does, however, make us want to be better and serves to reorient us with reference to the great superiority of the experimental method over empiricism. When all surgeons learn to ask: What is the evidence rather than who employs a certain procedure, then the absorptive capacity of surgeons for new found information will have been enhanced considerably. Surgery will profit immensely by having all surgeons listen to expositions in which the experimental method is employed. Moreover, young men prosecuting original researches have a right to be heard. And is it not a bit wearisome to have to listen to parrots of other men's thinking?

Unnecessary surgery. Some of my colleagues who are not surgeons tell me that some surgeons perform unnecessary operations and undertake necessary operations which they are not trained to do, for pecuniary gain. This is difficult for me to believe. If there be such men in our profession who call themselves surgeons, God have mercy on their souls! Is not the path of the well trained surgeon intent on doing the very best of which he is capable beset with difficulties enough? Can a surgeon take his tasks so lightly that he would submit patients, who seek his counsel to unnecessary or ill advised operations? God forbid! If this be true, every man in the profession, every hospital in the land should leave no stone unturned to expose such practice. We who enjoy the greatest confidences of patients who place their trust and lives in our hands have a sacred duty to perform. If we knowingly set aside that trust, we are not entitled to the protection which our medical license gives us. "If I forget thee, O Jerusalem, let my right hand forget her cunning." Steadfastness of purpose and consecrated devotion to his tasks should characterize the resolution of the surgeon in his outlook upon his work.

Surgery is a stern discipline. Surgery is an exacting and stern discipline. Let no man who aspires to be a surgeon be unmindful of this admonition. A realistic, critical attitude of self-analysis by the surgeon with reference to accountability for operative failures and postoperative complications is a *sine qua non* for continued growth and development of the surgeon and betterment of his accomplishment. The irrepressible optimism of the Pollyanish surgeon denies him the improvement and cultivation which comes from a critical review of every failure. At the base of most disappointments lie errors in judgment or execution, some neglect that might have been prevented with adequate forethought and preparation. Only when surgeons have succeeded in eliminating all *avoidable* causes of death after operation can they be satisfied with their own accomplishment—a laudable but unattainable objective. Yet, the struggle of striving to achieve that which lies beyond our reach makes us better surgeons for the effort. Any record, in which only *unavoidable* deaths account solely for the mortality, suggests that the surgeon and his associates have done their work well.

Improving the surgical mortality score. A consideration which must be always uppermost in a surgeon's mind is how to reduce the mortality score and at the same time extend the favors of surgery to those patients, who because of age or physical infirmity are not satisfactory operative risks. Familiarity with all the facets of the problem and a studied effort to eliminate or reduce to a minimum all the *avoidable* causes of death after operation are the items that make for an improved mortality record. In this endeavor the surgeon must exact a high standard of performance from himself as well as from his associates. The day of the one-man operation is over. It takes a trained team of surgeons and nurses, accustomed to working together and alert to the complexities and vagaries of a group of interrelated surgical problems to make a creditable showing. Limitless concern for every detail and precise execution of carefully planned procedures are items out of which success and improvement of the mortality score are compounded.

Preoccupation of mind of the surgeon. Because of the very nature of the cares and heavy responsibilities shared by surgeons, they come to have a certain preoccupation of mind. Try as we may, it is not easy to disguise completely our feelings when vexed with anxieties over ill patients. Those who know us best seem to be able to divine our true state of mind. The

cares of patients weigh heavily upon the mind of the surgeon and it is understandable that his spirits may exhibit some of the fluctuations of a barometer contingent upon how the patients under his care are getting on. Who among us has not felt a certain buoyancy of spirit when a very ill postoperative patient takes a turn for the better?

Static character of surgery made dynamic by synthesis of well known facts into new knowledge. This year marks the centenary of the first public demonstration of the employment of anesthesia for operations, one of the most beneficient and welcome gifts to mankind in the history of the world. Antisepsis and asepsis recreated surgery and opened up new and undreamed of avenues for the surgeon's skill. The exclusion of infections from clean wounds gave an impetus to surgery and the entire field of medicine, such as it has not experienced since. Surgery bounded forward with a terrific surge. Yet after some years, surgery appeared to have reached an impasse, such that, surgeons like the late Lord Moynihan were saying again, as surgeons of the preanesthetic and preantiseptic era had said, that surgery had reached the acme of its development along technical lines. Yet lesser innovations and a better understanding of the derangements in bodily economy attending operation have remade surgery again. The improvements that have come about in the last decade or more are not the startling variety that marked the swift progress which came with anesthesia and asepsis. Nevertheless, real improvement in many areas of surgery is readily discernible. The greatest forward strides probably have been made in intrathoracic surgery. Improved techniques in this province of surgery have permitted performance of operative procedures with low mortality rates for conditions which surgeons looked upon with hopeless discouragement and despair a generation ago. Vascular surgery of the thorax is a new chapter in operations being written by the surgeon of today, who has schooled himself in the stern discipline of preparing nice dissections of the large blood vessels of the thorax.

The gauge of a surgeon's accomplishment must be measured against the achievement for that period. It is unfair to compare the performance of a surgeon of one generation with that of another. There were good surgeons 25 years ago, but surgical organization in well appointed hospitals is much better today. Anesthesia is considerably better; our understanding of the nutritional requirements of surgical patients is far better and our knowledge of care of patients before, during, and after operation is better. Nursing care also is considerably better than it was a generation ago. We know more about shock and replace blood loss more adequately. We have learned that it takes time and patience to do operations well and that maintenance of a steady state of the patient throughout the operative procedure has done away with the necessity for hurry, a circumstance which condemned many an operation to failure, although the advocates of the method continued to insist it was the chief determinant in deciding whether a patient would survive.

In other chapters of surgery there has been less conspicuous but nevertheless noticeable improvement. Gastrointestinal surgery has been quite static for a generation. Yet, with similar improvements in technique which gave such accelerated momentum to the surgery of intrathoracic conditions, the last few years also have witnessed the extension of operations upon the gastrointestinal canal to older age groups and substandard risk patients with a constantly declining mortality rate. Apart from the items listed above which played so important a rôle in the flowering of intrathoracic surgery, an additional factor which has been of particular significance for the improvement of results in abdominal surgery has been increasing appreciation of the importance of suction applied to duodenal tubes to obviate the occurrence of intestinal distention following operation. Moreover, prevention of gastric retention precludes regurgitation into the lungs, a former frequent cause of postoperative pneumonia.

The discovery of the sulfonamides and penicillin has lent a great impetus to surgery, as it has to medicine as a whole. The discovery of a new fact can change the whole complexion of a problem. But how plodding a process is the discovery of a single new fact!

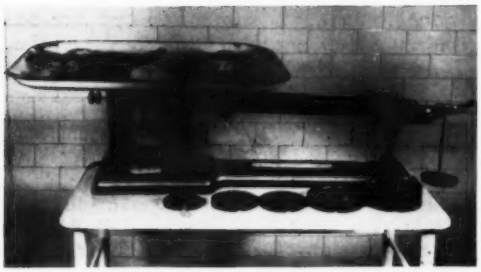


Fig. 1. Weighing scale employed in the general surgical operating rooms at the University of Minnesota Hospitals. Such a scale weighs to an accuracy of 1 gram. The use of dry sponges (save on exposed viscera such as small bowel or lung) serves to inform the surgeon of the blood loss at any juncture of the operation.

Little wonder that a new fact is a priceless possession and that we immortalize the names of men who have added a single important fact to knowledge. Keener appreciation of previously known facts lends its stimulus to a branch of knowledge; the impact of a new fact, however, gives impetus and momentum that is felt over a tremendous range; a new fact is like a ferment in changing a static state into a dynamic one. It breathes new life into an undertaking.

FORTUNES OF SURGERY

There is no equation or formula which can give a complete answer to the important question of what may be expected of an operation.

Fig. 3. Use of the Red-cross litter on a platform for patients who can not stand. This scheme of weighing needs the help of 2 nurses and an orderly to lift the patient, with least discomfort to him, onto the litter. (Surg. Gyn. Obst., 1941, Feb. 2A).

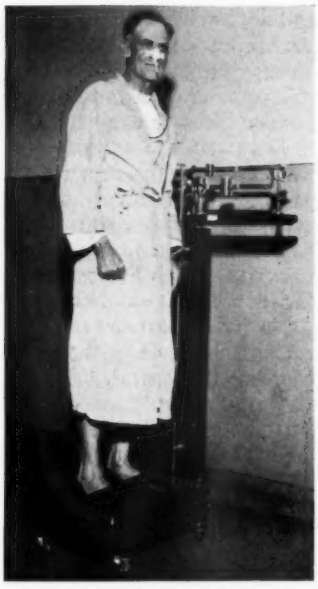
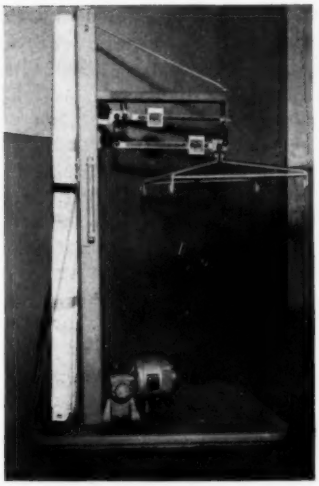


Fig. 2. Patients undergoing difficult operations can stand on a bedside weighing scale the day following operation. Patients are weighed in the morning before staff rounds, the gain or loss in weight from the preoperative weight helps to determine the water and sodium chloride requirements for the next 24 hour period.

The planning of the procedure, the nature of the organization in which the surgeon works, his training and his general outlook on his responsibilities, the character of the dissection he performs, the breadth of his comprehension of what constitutes satisfactory preoperative preparation and postoperative care, and the vigilance with which the anesthesists, the surgeon and his staff and the nursing staff watch over the patient—these are the determinants of the outcome of an operation. And yet even in this enumeration, some things are left to chance. On this latter score, may I say that the surgeon who leaves the care of a number of items to chance is an unsafe surgeon. No matter how well we have standardized the performance of a certain operative procedure, they are not all performed alike. The hemostasis in one operation may not be as satisfactory as we may have wished it; or the somewhat irregular placement of a single suture may have angulated an anastomosis whether gastrointestinal or vascular, such as



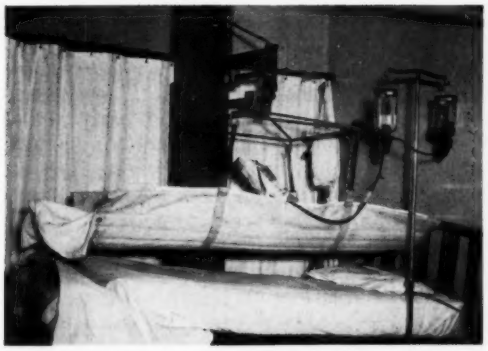


Fig. 4. a, A new bedside weighing scale built for me by Mr. John A. Phelan of the scientific apparatus shop. This scale, with an electrically driven motor to hoist the patient up and let him down, permits weighing the patient in bed. b, The scale in use. The hoisting device lifts the patient a few inches off the bed. There is no interruption of the administration of intravenously administered fluids.

to affect its function unfavorably. The performance of surgery demands a high level of concentration together with a harmonious coordination of eye, hand, and mind. Perhaps it was this circumstance that Thomas Fuller had in mind when he said the surgeon stands in need of "an eagle's eye, a lady's hand, and a lion's heart." For the difficult surgery of today, a sturdy pair of legs is also an indispensable necessity!

Fatigue undermines the surgeon's efficiency. There is no effective antidote for the fatigue and weariness which beset the surgeon in long and strenuous operative ordeals. Intentness of purpose urges him on to the performance of his best effort, though it cannot drive away the subjective feeling of fatigue and the physical impairment of efficiency which comes with long sustained application under trying circumstances. There are operations being performed now of such magnitude that the surgeon occasionally stands in greater need of postoperative treatment than the patient on completion of the operation! It is my feeling that an impetus may be lent to the safe conduct of patients through some of the more difficult and tedious operations, when university clinics come to attach greater importance to some of the techniques employed by industry and football coaches in combatting the inefficiency of fatigue by sending in a fresh team. No surgeon of experience will deny the deterioration of accomplishment which attends fatigue. The interests of the patient which should be the paramount concern in any operation, would be served better by such an expedient.

The great need of more precision techniques. Surgery and surgeons generally stand in serious need of greater precision techniques: in the gauging of patients as satisfactory risks for operation; in the assessment of whether the preoperative preparation is adequate; in the intricacies of the operation as well as in postoperative management. There is a mortality and morbidity of treatment as well as of disease! Let no surgeon mistake this. We are prone to say, the patient died despite all our efforts. How often the converse is true: the patient died because of what was done. Are we so blind or dull that we cannot see this? It is in the critical analysis of the events leading to unhappy outcomes that surgeons have the opportunity to improve themselves and to improve surgery.

We can all point out in our own experiences the repercussive effects of ill advised treatment. In this connection, I like to tell undergraduate students of an experience in which I was in a manner a participant. My family has a summer home not far from the Twin Cities. One of my neighbors is a veterinarian.

One summer before the long war years, we both had young dogs. My good friend, the veterinarian, said to me, his dog had manifested a few signs of distemper, and he was in the process of vaccinating him for it. Being a good neighbor, he volunteered to do as much for mine. I decided to let my dog take his chances with the distemper. He did contract it and was ill for a week or so, but made a complete and satisfactory recovery. A short time following our initial conversation, I asked the veterinarian how his dog was getting on. He said he feared he had overdone the vaccination of his dog and in consequence the dog's appetite was poor. As a stimulus to appetite, he was giving the dog some strychnine, and the dog was showing signs of improvement. A week later, our paths crossed again, and I asked the doctor how the dog was getting along. He said that the dog had been overtreated with strychnine causing him to have convulsions. In an effort to control the convulsions, he had anesthetized the dog with ether and had given him too much ether and had killed him! We, too, are guilty of occasionally shortening lives when we are striving to make them longer and happier. And often that rôle is not as self-evident as it was in this story.

How many patients lose their lives each year because of mismanagement of the water and electrolyte requirement of patients? To say many is an understatement. Is it happening in your clinic? It has in ours. I believe that when surgeons generally become more alert to the factors of safety in this intricate problem, they will have taken an important step forward in improving their own accomplishments. I shall not say very much about our general plan of management of this problem here, for I have discussed the problem at length elsewhere (2, 3, 4). I have the feeling, however, that when surgeons lend a more attentive ear to assessing such needs of patients in a more quantitative manner, they will be agreeably surprised to observe what great help such guides afford them.

Routine use of dry sponges in operations affords an opportunity to assess the gain in weight, thus informing the surgeon of the extent of the blood loss at any juncture of the procedure. To replace fluids in kind and in amount with that lost is obviously the best treatment. And to weigh patients before and immediately after operation, as well as in the convalescent period is the best of all guides in helping the surgeon orient himself with reference to the electrolyte and fluid requirements of his patient. Moreover, the weighing scale is far more sensitive in the detection of minor changes in body hydration than are changes in hemoglobin. Obviously such routine weighing of patients undergoing major surgery is often unnecessary, for the problem of hydration seems to resolve itself by employment of simpler means involving less trouble, constituting therefore needless effort. But who counts the cost of labor when lives are at stake? Do we not read almost daily in the newspapers of the heroic sacrifices of men, with no view to cost or personal danger, assuming large risks in the effort to save a life? In the hospital in which you work have lives not been lost because the surgeon and his staff were not alert to the changes occurring in hydration and electrolyte balance of the patients? We have lost patients needlessly through this agency, while professing an interest in the problem of water and electrolyte requirements of postoperative patients, at the same time, enlisting the helpful co-operation of the best talent that a University Clinic has to offer in the solution of such problems. It is in just such situations that the weighing scale has its chief virtue, in affording a prevision of what will happen if abnormal contractions or increases in body weight continue uncorrected. This I may also say: since the expedient of weighing patients undergoing major surgery has become routine practice on the writer's surgical service, loss of life through disorientation of the surgical staff with reference to the important problem of hydration of patients has been more than decimated. I must confess we still go astray occasionally but usually recognize the errors of our ways before disaster overtakes us. It is in the surgery of elderly substandard risk patients, who tolerate abuses poorly and especially in the surgery of gastrointestinal conditions necessitating the presence of inlying duodenal tubes, that the weighing scale is a

sine qua non, if the surgeon aspires to do such operations with risks not far out of line with those assumed by younger standard-risk patients. Reducing the mortality score, as I stated previously, consists essentially in the recognition of error and its correction. If a patient's weight in the early postoperative phase can be maintained within 2 to 3 per cent of the preoperative value (plus or minus), the surgeon is assured that the water and electrolyte requirements of his patient are being met satisfactorily. Pneumonia and cardiac failure as a consequence of overhydration, owing largely to the administration of too much sodium chloride, we saw not infrequently postoperatively among older patients undergoing extensive and complicated surgery, before routine employment of the weighing scale. Routine weighing of such patients to detect deviations from the preoperative normal is at least as important as taking the patient's temperature. When surgeons learn to deal satisfactorily with the difficult problem of hydration of postoperative surgical patients, one of the most formidable of hazards to safe conduct of the patient through operation will have been surmounted. It is a barrier to recovery from operation that the surgeon must learn to hurdle.

Mr. Albert Sullivan Jr.,[1] in studying the case records of 151 consecutive patients undergoing major surgery upon the gastrointestinal canal, during the first 6 months of 1946, observed that in this group slight losses of weight were far more common than gains in weight. Only 11 patients (7.3 per cent) showed a weight gain of 2.5 per cent of their total body weight, whereas 76.8 per cent exhibited weight losses of 2.5 per cent or more. The greater number of this group lost weight during the first 5 days after operation. Only 1 patient lost more than 6 per cent of the body weight. The average age in this group of patients was 58.9 years. These findings suggest that our surgical staff is more sensitive to weight gains than losses in weight. All of the patients in this group had inlying duodenal tubes, presenting therefore essentially, the most difficult problems of maintenance of water and electrolyte equilibrium. Obviously, the cause of the weight loss in most instances was administration of too little sodium chloride accompanied by employment of moderately generous quantities of 10 per cent glucose solution. The effect of such therapy is to promote diuresis, a circumstance that is pleasing to surgeons, especially when dealing with a group of patients whose mean age is high. Needless to say, it is important to take careful note of small deviations from the preoperative weight, in order to keep fluctuations in weight at a minimum. Of the total measurable output of body fluid, 70 per cent was urine, the remainder being constituted largely by the fluid aspirated by the inlying duodenal tube. The average daily administration of sodium chloride was 6.5 grams in the early convalescence of those patients losing 2.5 per cent or more of their body weight. These observations suggest that the daily administration of 6.5 grams of sodium chloride is probably slightly less than enough for patients with inlying duodenal tubes undergoing major surgery upon the gastrointestinal canal.

Acquaintance with and employment of precision techniques by the surgeon and his staff in the various items that hedge about an operation afford the patient the best promise of a favorable outcome. It is the operation without mishap and a convalescence without complication that spells success. Such a procedure also permits early ambulation and early dismissal from the hospital. The convalescence punctuated by complication is synonymous with increased morbidity as well as mortality. The circumstances which characterize success and failure are often "minor differences"; but it is out of infinite and alert attention to detail that success is compounded. By very dint of relentless perseverance in his attack upon the factors that constitute the "minor differences" between success and failure, the surgeon can gradually overcome the hazards that are undermining his efforts. Recognition of error, when accompanied by a resolute determination shared by the surgeon's staff to avoid the repetition of such mistakes, is the best assurance against failure. It is a source of ever recurring wonder to me how well patients get on after serious operations un-

[1]Medical student from Tulane, doing a voluntary externeship on the surgical wards during the summer of 1946.

attended by complication. And when surgeons succeed in making the unpleasant trials of the waking and recovery periods following operation more agreeable, patients will be less likely to regard an operation as a journey "through the valley of the shadow of death."

SUMMARY AND CONCLUSIONS

"Order is heaven's first law." It also must rank among the most important of guiding principles in the surgeon's code. Without order the results of operation are unpredictable. A surgeon who has regulated his activity in accord with semblance of good order comes well prepared for operation. Preparation has to do with readiness as well as fitness. He does not undertake operations for which he is not prepared. Nor does he perform unnessary operations. The surgeon's trust is as sacred as life itself and must not be profaned. The surgeon who has schooled himself in the preparation of nice and precise anatomical dissections does not permit himself to be hurried. He places the safety of his patient above every other consideration. And the security of the patient demands not alone that, the surgeon watch over him with tender and observant care during operation but that the surgeon has seen to it that no detail is overlooked in the preoperative preparation, and that alertness and vigilance characterize the care of the patient after operation.

The success of operations depends upon a harmonious blend of many things. The practical wisdom garnered from experience is in essence an issue resulting from detection, acknowledgment, and correction of error. Though we falter, if we are in earnest in our determination not to fail, success is inevitable. We must learn to count the cost less and value the result more. The surgeon's objective should be the elimination of all *avoidable* causes of death after operation. The safe conduct of the patient through operation is a matter upon which an instruction can be given more readily than consistently followed. Portia's prudent counsel in the "Merchant of Venice" on this score is well known to you. She said, "If to do were as easy as to know what were good to do, chapels had been churches and poor men's cottages princes' palaces." It is a good divine that follows his own instructions. I can easier teach twenty what were good to be done than be one of the twenty to follow mine own teaching. The fortunes of our patients are determined by the manner in which the formalities of surgery are heeded by the surgeon. The functions of surgery and its future growth as a benevolent and helpful aid to man suggest that improvement in accomplishment demands that the surgeon be mindful and observant of the stern disciplines of his handicraft.

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CLINICAL USES OF STREPTOMYCIN IN MEDICINE AND SURGERY

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ALTHOUGH streptomycin was first described by Schatz, Bugie and Waksman less than 3 years ago, the drug is already in full commercial production and distribution and has proved to be a useful antibacterial agent in medical and surgical practice. The full possibilities and limitations of streptomycin treatment in several important diseases remain to be determined but progress has been extremely rapid in the last 2 years and should continue at an accelerated rate.

The usefulness of streptomycin is dependent on the fact that this antibiotic agent is effective against several pathogenic bacteria which are not susceptible to the action of other antibacterial substances. These bacteria include some frequently encountered gram-negative bacilli and above all the bacillus of tuberculosis.

The treatment of infections of the urinary tract due to bacteria sensitive to streptomycin has been extensively studied (7, 9), and it is uniformly agreed that streptomycin is of value in such treatment although its potentialities are limited. These bacteria frequently acquire a resistance to the action of streptomycin within a few days; hence, if permanent results are to be realized, it is extremely important that conditions favorable to persistence or recurrence of infection be corrected promptly, if possible. Strains resistant to streptomycin are more likely to be developed if there is obstruction to flow of urine or if calculi or other anatomic defects permitting survival of bacteria are present. The importance of proper timing of treatment in relation to surgical intervention becomes obvious.

Bacteriemia due to gram-negative bacilli sometimes occurs, especially in association with severe infections of the urinary tract and as a postoperative complication following operation on the infected urinary tract. Streptomycin therapy frequently is effective in treatment of such bacteriemia (7, 9) when due to organisms sensitive to this antibiotic agent (9).

Meningitis due to sensitive micro-organisms, especially gram-negative bacilli, should be treated with streptomycin, utilizing both parenteral and intrathecal routes of administration. My associates and others (7, 9, 10) have reported favorable results in influenzal meningitis treated with streptomycin.

Since acute peritonitis is frequently of such serious portent and due to such an admixture of pathogenic micro-organisms I would recommend the simultaneous use of all available antibacterial agents in medical treatment. The combination of streptomycin with penicillin appears to be thoroughly logical under these circumstances, especially if the peritoneal cavity is soiled with intestinal contents.

Wound infections due to mixed bacterial flora should frequently be treated with both penicillin and streptomycin, especially if bacteriologic examination proves the presence of sensitive micro-organisms. Fully adequate débridement should first be carried out to minimize the possibility of a recurrence of the infection due to bacteria which have acquired a resistance to the action of streptomycin.

Streptomycin is of real value in some cases of chronic suppurative pulmonary disease, such as bronchiectasis (11), and especially as a preoperative measure preparatory to pulmonary resection. Here again it should usually be used in conjunction with penicillin and administered as an aerosol. The duration of treatment will vary from 1 to 2 weeks or more, the treatment being continued until sputum is reduced in amount, changed in character and rendered bacteriologically sterile or nearly so. Cases of bronchiectasis suitable for streptomycin therapy may be selected by merely ex-

From The Division of Medicine, Mayo Clinic.

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amining smears of the sputum stained by Gram's method. If numerous gram-negative bacilli are present, streptomycin is likely to be a useful adjuvant to penicillin therapy.

Acute and chronic infections of the respiratory tract due to organisms of the Hemophilus and Klebsiella groups may be treated successfully with streptomycin (7, 9).

The treatment of tularemia with streptomycin has yielded spectacular and promptly curative results (5). Streptomycin may be considered a specific remedy for tularemia; hence the accurate diagnosis of tularemia becomes of greatly increased importance.

Brucellosis and typhoid fever are caused by organisms which are only moderately sensitive to streptomycin. The latest available reports of streptomycin therapy in these diseases are not encouraging (9) except possibly during the most acute phases with demonstrable bacteriemia.

When streptomycin is administered orally it is not absorbed from the alimentary tract in significant amounts; hence its oral administration is useless for treatment of systemic infections. However, the antibiotic agent is not destroyed but remains within the lumen of the bowel to exert its antibacterial effect on the intestinal flora (6). The possibilities of orally administered streptomycin have not been fully studied for preoperative preparation of patients prior to intestinal operation, either as a substitute for sulfonamides or in combination with sulfonamides. My surgical colleagues have made sufficient use of streptomycin in this manner to indicate that it does have practical possibilities.

The action of streptomycin on cultures of Mycobacterium tuberculosis was noted early (13) but this is a property which had been described previously for a number of other substances of microbial origin (4) and many synthetic chemical compounds (14). When streptomycin proved to be extremely effective against experimental tuberculosis of guinea pigs (2, 3), its clinical possibilities were recognized and quickly explored.

The greatest potentialities for streptomycin therapy appear to exist in treatment of tuberculosis (8), including some surgical types of tuberculous infection. This is due to the fact that no other practical and effective antibacterial therapy is available against the bacillus of tuberculosis and to the fact that this bacillus is much more sensitive to streptomycin than are the other common pathogenic bacteria. Furthermore, the tubercle bacillus remains sensitive to streptomycin for at least a few months before becoming drug resistant (15) and this permits realization of satisfactory therapeutic effects, especially in lesions of recent origin. It also has been found that some rather poor candidates for radical surgical treatment of pulmonary tuberculosis may be rendered excellent candidates after a few months of treatment with streptomycin. Likewise postoperative tuberculous complications may be amenable to streptomycin therapy or may be prevented by use of the drug.

Many types of tuberculous infection unfortunately produce destructive changes which no drug can directly benefit. Antibacterial therapy is only suppressive in this and other diseases and will yield permanent benefits only if natural mechanisms of healing can achieve supremacy during the limited period of a few months during which the bacilli are sensitive to the action of streptomycin. Selection of tuberculous patients for streptomycin treatment must be undertaken with the greatest care. During the past 2 years my colleagues and I have followed a few simple rules, based on our concept of the action of streptomycin. These rules may be enumerated as follows: (1) Patients who are making satisfactory progress on conventional forms of treatment for pulmonary tuberculosis or who are likely to do so should not receive streptomycin. (2) Patients who have terminal types of pulmonary tuberculosis, especially when bilateral destructive changes are present, and who could not become candidates for surgical treatment are not regarded as good subjects for streptomycin treatment. (3) Patients who have old chronic nonprogressive fibrocaseous and cavernous types of pulmonary tuberculosis are not likely to experience satisfactory results and hence should not be treated. (4) Priority in treatment has been given to more acute, progressive pulmonary tuberculosis of recent origin. In general, patients with most severe constitutional symptoms and with least destructive

pulmonary changes have obtained the best results from streptomycin treatment. These are individuals with naturally low resistance, or with depleted resistance, and hence those most in need of assistance from antibacterial therapy. It should be repeated that such treatment should be given before the disease has wrought changes in the lung such as cannot be repaired within a few months. All patients with pulmonary tuberculosis chosen for streptomycin treatment should have a component of exudative disease, and the larger the proportion of exudative to proliferative tuberculosis the better.

The clinical results of treatment of such patients often are realized promptly. Within the first few weeks fever declines, cough and expectoration decrease, appetite and a sense of well-being return and the patient begins to regain lost weight. Later, after 6 to 8 weeks of treatment, roentgenographic evidences of improvement of exudative lesions are first noted. Usually within 3 to 5 months maximal clinical and roentgenographic improvement has been attained. This would appear to be the time for surgical treatment of remaining disease and especially for closure of any remaining cavities, such as might serve as sources for subsequent bronchiogenic dissemination of the disease.

Ulcerating tuberculous lesions of the larynx, the hypopharynx and the tracheobronchial tree have healed rapidly and so far without exception in our small series of 10 cases. These patients have received combined treatment with intramuscularly administered streptomycin and streptomycin aerosol.

Some types of extrapulmonary tuberculosis have responded to streptomycin treatment with remarkable uniformity. This is especially true of chronic long standing draining sinus tracts, which usually close within a few weeks, but these will remain closed only if treatment is continued for several weeks after apparent healing. In renal tuberculosis and tuberculous cystitis, temporary and palliative effects have been observed frequently but actual healing of renal lesions has been observed rarely, possibly because the kidney lacks the power to heal tuberculosis readily. In only a few cases of tuberculosis of bones and joints has streptomycin been used but results have been encouraging. Much remains to be learned about streptomycin in relation to orthopedic surgery in the treatment of tuberculosis of the skeletal system.

Until the advent of streptomycin there was no way in which the course of tuberculous meningitis and miliary tuberculosis could be modified. Even with streptomycin treatment there is an extremely high mortality rate. However, in most cases of early tuberculous meningitis the patients respond promptly to adequate intramuscular and intrathecal streptomycin treatment but all too frequently these gains are not permanently sustained. At least temporary clinical remission is almost the rule following streptomycin treatment of early but acute and severe tuberculous meningitis. Consciousness is regained, often within a few days, fever declines within a few weeks, a sense of well-being returns and frequently patients appear to be essentially normal, even for several months. Subsequent exacerbations of the disease are likely to recur and not to respond to treatment. However, this may not always be true, for in 3 cases of proved tuberculous meningitis arrest of the disease continued for several months following discontinuation of a 6-month course of intensive treatment. One patient has no residual neurologic signs, one is normal except for deafness, and the third has apparently received severe damage to the central nervous system, especially the cerebellum. Although nearly a year has passed since the onset of illness in these 3 cases, it is too early to classify the patients as cured. Five patients who had tuberculous meningitis have died despite treatment but 3 of these did not receive what is now regarded as adequate treatment and the remaining two were first seen at a late stage of the disease.

Disseminated hematogenous tuberculosis of miliary type has not responded previously to any form of treatment and spontaneous recoveries have been extremely rare. With streptomycin treatment it is possible to bring about a complete clinical and roentgenographic remission in a large proportion of cases but, unfortunately, the recurrence rate has been very high thus far and three of our four treated patients have eventually died. The remaining

patient has remained well for 6 months but cannot yet be classified as cured.

Tuberculosis of the alimentary tract and tuberculous peritonitis have not been studied adequately but symptomatic improvement of the 5 patients who have been treated at the Mayo Clinic has been striking.

Although clinical effectiveness of streptomycin is readily demonstrated in many types of tuberculous infection, the results are often not permanent and frequently do not compare with results achieved in acute diseases treated with other antibacterial agents such as penicillin. The limitations of streptomycin treatment in tuberculosis must be emphasized constantly in this day of "miracle drugs," and the emphasis must still be placed on the known effective methods of treating tuberculosis, especially care in a sanatorium and collapse therapy. The place of streptomycin in tuberculosis therapy has not been determined, but this agent is much more likely to supplement than to supplant the proved effective standard methods of treatment.

Streptomycin usually is administered by intramuscular injection, doses being given every 3 to 4 hours and totaling from 1 to 3 grams per day. The lower limits of effective dosage have not been fully explored nor can final statements be made concerning the upper limits of safe dosage. Streptomycin is more toxic than penicillin but very little difficulty is experienced in treatment of more acute diseases which require only a week or two of treatment. When treatment is continued beyond 2 to 4 weeks nearly all patients will experience some disturbance of equilibrium (1), occasionally to a severe degree. Fortunately, compensation is achieved in all or nearly all instances, more promptly in younger than in older patients, and no permanent disability is likely to result. Sluggish response to caloric stimulation of the vestibular apparatus is usually noted for many months and perhaps permanently, even when there is no residual functional disability. The cause and significance of these changes have not been determined fully and are in need of complete investigation. Deafness has been noted occasionally but hearing is ordinarily regained if treatment is discontinued promptly. In this respect, streptomycin resembles such drugs as quinine and salicylates. Evidence of renal irritation has been noted occasionally but serious renal damage is not nearly so likely to occur as is true with administration of sulfadiazine. Streptomycin should be used with caution when there is reason to fear pre-existing impaired renal function because the drug may not be readily excreted under these conditions.

SUMMARY

Streptomycin is an effective antibacterial remedy of value in treatment of several infectious diseases not amenable to treatment with other antibacterial substances.

Streptomycin may be used in combination with penicillin for treatment of mixed infections such as are likely to occur in the presence of acute peritonitis, chronic suppurative pulmonary disease and contaminated wounds.

Streptomycin has value in treatment of infections due to gram-negative bacteria occurring in the blood stream, in the meninges, or in the urinary tract.

Streptomycin is highly specific in treatment of tularemia. It has but little value in treatment of brucellosis and typhoid fever.

Streptomycin is the only practical antibacterial substance which is useful in treatment of tuberculosis. Limitations of streptomycin therapy in this disease appear to be imposed by the destructive and granulomatous changes produced in tuberculous tissue and by the fact that the drug cannot be depended on to destroy tubercle bacilli in the human body.

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THIOURACIL AND IODINE

The Preoperative Management of the Thyrotoxic Patient

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FROM the reported experiences in the collected literature, 3 salient characteristics of thiouracil therapy have been emphasized. These have been the prompt clinical response to the drug; the standardization of the dosage at 0.6 gram, daily by which the basal metabolic rate is reduced 1 per cent each day; and, most important, that thiouracil toxicity has appeared in about 14 per cent of all patients so treated.

Since so much value, yet so much danger has been found in the treatment of the thyrotoxic patient with thiouracil, some safer method of management should be sought to obtain the maximal therapeutic effect of the drug with the greatest margin of safety. This has been the objective of the present study, an admittedly small series, since from a total experience of 527 thyroidectomies, only 20 recent hospital cases were considered suitable for this form of therapy.

There were 16 females and 4 males varying in age from 23 to 76 years. The average age of 45.1 years was equivalent to that of 190 thiouracil treated patients reported by Lahey. In the series were 9 nodular and 9 diffuse goiters and 1 recurrent goiter in each group. The tissue submitted from the recurrent diffuse goiter was reported by the pathologist as adenocarcinoma. All admission basal metabolic tests were made after at least one day of rest in bed. The highest was plus 72.4 per cent and the lowest plus 25.1 per cent; the average plus 43.57 per cent. This approximated Lahey's average of plus 49 per cent. Admission leucocyte counts ranged from 10,050 to 4,150 with an average of 7,135. All other clinical laboratory determinations and radiological examinations were performed routinely on admission but have been omitted from this report. Medication was withheld until the laboratory findings were charted. Bed rest, except for 2 hours daily was the rule. In addition, ice caps were applied to the head and precordium; intravenous fluids were administered as indicated and sedation obtained by the generous use of phenobarbital. The average daily dose of phenobarbital was 4 grains. This included the larger doses of 3 grains to 9 grains given the night before operation. While the Bartletts have advocated larger amounts to produce narcosis and "semi-anesthesia" these patients were easily managed on the smaller dosages since avertin was used as a basal anesthetic 45 minutes before the scheduled operating time. All patients received 0.6 gram of thiouracil daily divided into 3 doses each of 0.2 gram. The longest period of administration was 21 days, the shortest 6 days, and the average 11.9 days. There were 4 exceptions to this dosage. In 3 patients it was necessary to increase the amount, and in 1 to decrease it. In Case 8, patient previously iodine resistant, required 0.6 gram daily for 8 days, 0.8

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TABLE I.—THIOURACIL—WHITE COUNTS—ALL DIFFUSE GOITERS—10 CASES

No.	Admission and weekly counts			
7	9200	7300	7000	5950
8	4900	6650	6600	
9	4000	6050	4300	
10	10050	11200	13500	
11	5550	7450		
12	9600	9100	6950	
13	6350	8450	6000	
14	9900	13450	10600	
17	5650	5000	7850	5900
19	7500	5450	10050	8900

TABLE II.—THIOURACIL—WHITE COUNTS—ALL NODULAR GOITERS—9 CASES

No.	Admission and weekly counts			
1	4150	5300	3250	7700
2	6300	6200		
3*	7200	6000		
4	7650	6100		
5	7200	8050	7350	5400
6	8400	9400	9500	
15	7100	3600	4950	5900
16	5750	4900		
20	5650	5000	7850	5900

*Recurrent.

gram daily for 5 days and 1.0 gram daily for 5 days to obtain the desired effect. In Case 4, 0.6 gram was given 4 days, 0.8 gram for 2 days; in Case 6, 0.6 gram was given 6 days and 0.8 gram for 2 days; in Case 7, 0.6 gram was given for 11 days and 0.4 gram for 4 days.

Since the clinical toxicity of thiouracil was reported to the profession soon after its introduction, every patient was carefully observed and interrogated daily so that side effects could be promptly noted and immediately treated. Further, leucocyte and differential counts were obtained at least every 7 days.

When the weekly counts in 10 patients with diffuse goiter were tabulated no instance of leucopenia or agranulocytosis was noted (Table I). In this tabulation, leucocytosis appeared to be a response to thiouracil in several instances.

In 2 of the 9 nodular goiters (Cases 1 and 15), a reduction of white blood count occurred but in neither did it drop below 3,000, the arbitrary level of leucopenia (Table II). In both patients, the leucocyte response returned to safe levels despite the fact that thiouracil therapy was continued. Similar increases in the white cell count in thiouracil treated patients have been reported by Astwood.

In Case 18, patient had been previously operated upon 8 years ago, a recurrent diffuse toxic goiter was admitted with a basal metabolic rate of plus 42.1 per cent and a pulse rate of 100. The white blood count was not affected after 15 days of treatment with thiouracil—admission and weekly counts being 7250, 7300, and 7350. The pathologist reported the tissue to be that of an adenocarcinoma.

In the graphic representation of the leucocyte counts, two definite patterns of response to thiouracil therapy occurred. Exactly 50 per cent of this series showed an initial reduction in white cells which was followed by a rise to the admission level or above.

In the other 50 per cent a prompt increase in leucocytes was noted. This was either maintained or fell below the admission count. Analysis of the individual curves revealed that nodular and diffuse goiters were equally represented in each chart. Further, it was evident that the reductions were transitory. Agranulocytosis was not observed and all patients were free of any manifestation of thiouracil toxicity.

The clinical response to thiouracil in this group was manifested by loss of irritability, restlessness, emotionalism and tremor. The reductions in the basal metabolic rate were marked, and thiouracil was discontinued as soon as the rate was recorded at plus 30 per cent or below. The average basal rate at the time of discontinuance of thiouracil was plus 15.8 per cent.

Since the thyrotoxic patient with a basal rate of plus 15 per cent to plus 30 per cent has rarely failed to benefit from rest, sedation and iodine in the past, a rate of plus 30 per cent or below was arbitrarily set for the administration of iodine. Lahey (3) suggested its use in thiouracil treated patients for the purpose of avoiding excessive operative hemorrhage from a hyperplastic gland. In order to obtain the greatest iodine saturation in the shortest time, 60 drops of Lugol's solution in cream were administered each day, a practice which has been followed without untoward effect for many years. The average length of iodine administration was

6.2 days. Thyroidectomy was performed without incident and without postoperative storm in all cases. In Case 5, a large nodular intrathoracic goiter in a patient aged 65, the admission basal rate was plus 31.3 per cent and grave myocardial damage without heart failure was present. The rate was reduced to plus 14.2 per cent by thiouracil and patient was then iodinized. Death occurred less than 30 minutes after the incision was made as the right lobe and isthmus were removed. This was a cardiac death in the thyrocardiac group which is known to carry the highest mortality rate.

Since end-results and the time spent in a hospital have always been pertinent factors, this form of management should be compared with present methods of combined ambulatory and hospital care. Thiouracil was used an average of 11.9 days, plus Lugol's solution 6.2 days, or a total preoperative time of 18.1 days. Case 5, the operative death and Case 20 in which patient refused operation have been deducted from these figures. The average postoperative time was 6.8 days, or an average total hospitalization of 24.9 days. During all of this time, each patient was under medical control while receiving a known toxic drug. This control cannot be exercised over out-patients having at their personal disposal 1 or 2 weeks' supply of thiouracil. Until thyroid disease can be cured medically, the thyrotoxic patient must eventually come to operation. While the standard 0.6 gram daily dose of thiouracil effectively reduced the basal metabolic rate, this small series of 527 thyroidectomies and the thousands reported elsewhere have clearly pointed out that Lugol's solution, bed rest, and sedation, as well as thiouracil, are still factors essential to the successful management of the thyrotoxic patient.

SUMMARY AND CONCLUSIONS

1. Thiouracil has a field of usefulness and should be limited to the preoperative preparation of the thyrotoxic patient.

2. The dangers which have been previously reported appear to be due to the prolonged use of a potent drug.

3. These dangers can be minimized in the hospital by careful observation, study, and the individualizing of treatment to the needs of each patient.

4. It would seem unwise to place in the hands of an out-patient, a dangerous drug and allow such a patient to be removed from regular and controlled observation.

5. The use of iodine in conjunction with thiouracil is a sound and safe practice since it eliminates uncontrollable operative hemorrhage and thus ensures safe hemostasis.

6. Reduction of the basal metabolic rate to limits between plus 15 per cent and plus 30 per cent by thiouracil, followed by the administration of large doses of iodine, reduces the preoperative preparation time to the economic advantage of the patient without materially increasing the surgical risk.

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FLUID AND ELECTROLYTE BALANCE

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WITH the rapid extension of knowledge of fluid equilibrium changes in disease, the fundamental therapeutic philosophy that seems most appropriate to the problem has been clearly stated by Butler and Talbot. "Until information pertaining to these and other factors concerned with the optimal utilization of parenterally administered nutrients is available, the prescription of the rate of infusion and composition of parenteral fluids for a given patient must reflect common sense, careful clinical observation, and a tolerance indicative of an enlightened awareness of ignorance."

During the past two decades much effort has been expended in attempts to place the diagnosis and treatment of "dehydration" upon arithmetical bases. All the methods that have been suggested have been based upon the mistaken assumption that various blood solutes (Na, Cl, and plasma protein) and suspended particle (red blood cells) volumes were approximate constants.

Consequently, even though great emphasis has been placed upon laboratory methods for "controlling water balance," there are no universally applicable or dependable laboratory-based formulae available for the detection and treatment of fluid disequilibrium states. Therefore, a clinical plan of procedure appears to be more generally applicable to the problem. Although the plan of procedure described leaves much to be desired, it has been found to work in a relatively successful manner.

The correlation of the history and physical signs is the first step taken in the formulation of a presumptive clinical understanding of the type of fluid disequilibrium state present. The states that may exist are listed in Table I. It is obvious that there are many possible combinations of water and salt disequilibria.

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TABLE I.—DISTURBANCES IN FLUID EQUILIBRIUM

Water disturbances	*Extracellular salt water disturbances*
1. Volume.	1. Volume. (Changes in relation of extracellular salt water volume, base content of body, to total body solids.)
a. Deficit. (The water content of the body in relation to total solids is diminished.)	a. Deficit. (Base deficit,* sodium deficit.)
1. Acute.	b. Excess. (Base excess,* sodium excess.)
2. Chronic.	2. Composition. (Departure from the electrolytic pattern of "normal" extracellular fluid.)
b. Excess.	a. Acidosis. (Alkali deficit,* bicarbonate deficit.)
1. Absolute. (The water content of the body in relation to total solids is increased.)	b. Alkalosis. (Alkali excess,* bicarbonate excess.)
2. Relative. (The water content of the body is increased in relation to the mobile sodium content. The actual water content of the body in relation to total solids may be in excess, normal, or in deficit.)	3. Distribution. (Reciprocal variations in the extracellular salt water volume of various tissues with the total extracellular salt water volume remaining constant—e.g., other tissues lose extracellular salt water to the skin when it is injured.[1])

*Peters and Van Slyke (16).

[1]Reciprocal variations in the volume of distribution of sodium in relation to the solids of various tissues.

However, the common types of fluid disorders are relatively few in number (Table II).

Acute water deficit. (Primary water deficit with an increased solute concentration of body fluids, Fig. 1.) Sudden complete cessation of oral water ingestion is the usual clinical cause of acute water deficit. The deficit of water pro-

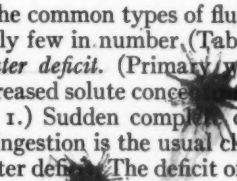

Fig. 1. At left, normal extracellular fluid; at right, acute water deficit.

TABLE II.—CLASSIFICATION OF CLINICAL DISORDERS OF FLUID AND ELECTROLYTE BALANCE*

Water disequilibria	*Salt disequilibria*
1. Acute water deficit.	1. Extracellular salt water deficit.
2. Chronic water deficit.	2. Extracellular salt water deficit with water deficit.
3. Absolute water excess.	3. Extracellular salt water deficit with relative water excess.
	4. Extracellular salt water excess.
	5. Extracellular salt water excess with relative water deficit.
	6. Extracellular salt water distributional shifts.
	7. Any of above (1, 2, 3, 4, 5, 6) with changes in base-bicarbonate (alkalosis or acidosis).

*Intracellular salt disequilibrium states are not considered in constructing this table.

gresses at a rate rapid enough to prevent the kidney from excreting salt in sufficient amounts to maintain the solute concentration of the body fluids at a normal level. This state is accompanied by intense thirst if the individual is conscious. The clinical signs that accompany acute water deficit are: oliguria, dryness of mucous membranes, elevation of body temperature (rectal), and hallucinations, disorientation, mania, and coma in order of progression of the deficit. The laboratory signs are: a high urine specific gravity (if renal function is good), high blood urea, and concentration of red blood cells, plasma proteins, chloride and sodium in the blood.[1] The correlatives necessary for making the diagnosis are: the physical signs of water deficit, a high urine specific gravity, and the absence of signs of an extracellular salt water volume deficit (see extracellular salt water volume deficit).

Chronic water deficit. (Primary water deficit with a normal solute concentration of body fluids, Fig. 2.) Chronic water deficit is the most frequently encountered disturbance of fluid equilibrium in psychiatric institutions. It differs from acute water deficit because a compensatory renal excretion of salts (Na and K) occurs as the body content of water falls (4). This tends to maintain the solute concentration of body fluids within normal limits. However, salt concentrations finally rise when the deficit of water becomes so great that insufficient water is provided to the kidney to excrete the salt necessary to keep solute concentrations normal.

[1]Note especially that diminished elasticity of the skin, softening of the eyeballs, and longitudinal wrinkling of the tongue are not listed as signs of acute water deficit.

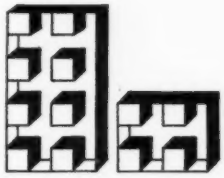

Fig. 2. At left, normal extracellular fluid; at right, chronic water deficit.

In the treatment of chronic water deficit one must remember that salt deficit is associated with the water deficit even though no obvious loss of salt by vomiting, diarrhea, or sweating has occurred.

The cause of chronic water deficit is a decrease in the rate of water accretion of such a degree that the rate of total water gain is less than the rate of minimal water loss. However, the discrepancy between the gain and the loss of water is not so great as to prevent the kidney from holding the solute concentrations of body fluids within the ranges compatible with health.

The most frequent cause of the disorder is a reduction in the sensorium that under conditions of health keeps the water content of the body within a relatively narrow range of variation. Its frequency of occurrence is high in psychopathic states, organic brain disease (senile, alcoholic, luetic, postapoplectic), drug addiction, chronic febrile illnesses, geographic limitation of water intake, and chronic painful states (peripheral vascular disease, causalgia, chronic infection, arthritis, and neoplasia).

The clinical signs of chronic water deficit are predominantly those of an extracellular salt water (base) deficit provided that the development of the deficit proceeds slowly enough for the kidney to keep the solute concentration of the body fluids constant. However, the signs of acute water deficit may be added to those of extracellular salt water defi-

cit whenever the solute concentrations of the body fluids rise. Eating diminishes as the deficit increases, so that the management of undernutrition is difficult unless cognizance is taken of the fact that the intake of food decreases as the deficits of water and salt develop.

The correlatives necessary to make a diagnosis of chronic water deficit are: physical signs of an extracellular salt water deficit, chloride in the urine, and a high urine specific gravity (>1.020 if renal function is good). Blood solute concentrations may be normal or high. The blood content of urea is increased.

Absolute water excess. (Water content of the body in relation to total solids is increased, Fig. 3.) Accretion of water at rates greater

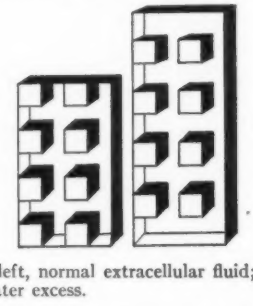

Fig. 3. At left, normal extracellular fluid; at right, extracellular water excess.

than the maximum capability of excretion is the cause of this disturbance. In a healthy adult man the rate of accretion must exceed 800 to 1,300 (17)[1] cubic centimeters per hour. However, the maximum capacity of renal water excretion diminishes and may actually approach zero under certain conditions,[2] so that water excess can develop with relatively slow rates of water intake. The change from a positive to a negative correlation between water gain and loss may be spontaneous (drinking more than can be excreted) or forced (intravenous injection of glucose in water faster than it can be excreted). The spontaneous development of water excess may be seen following hemorrhage[3] and traumatic shock (femoral shaft fractures, burns [22], crush injuries), during and following recovery from prolonged and deep general anesthesia especially if hypotension has been present, and following the administration of pituitrin to persons suffering from diabetes insipidus (25).

Apparently most of the signs and symptoms of absolute water excess (water intoxication) have two origins (18), an increased intracranial pressure and an increase in the rate of extrarenal and extracutaneous water excretion. The signs and symptoms that seem to be related to an increase in intracranial pressure are: an increase in spinal fluid pressure, papilledema (if significant water excess has existed for more than 36 hours), muscle twitching, headache, anorexia, nausea, vomiting, bradycardia, elevation of blood pressure, dimness of vision progressing to blindness, and convulsions with interval coma. The signs and symptoms related to an increase in the rate of water excretion via extrarenal and extracutaneous channels are: salivation, lacrimation, diarrhea, and nonprojectile productive vomiting. Body temperature changes are variable; they appear to be more intimately related to the illness with which the water excess is associated than to the state of water intoxication *per se*. A definite, soft, rapidly disappearing, subcutaneous pitting edema is rarely seen. The cutaneous sign of an excess of body water is intracutaneous rather than subcutaneous edema. Pressure on the skin over bone produces a slowly disappearing, depressed fingerprint of the examining finger. Occasionally the imprint may last for 15 minutes. The laboratory signs of water excess are: a low urine specific gravity, a low urine chloride concentration, dilution of serum solutes, and a low hematocrit.

Extracellular salt water deficit. (Reduction of body content of base, Fig. 4.) Extracellular salt water deficit rarely exists alone. It is gen-

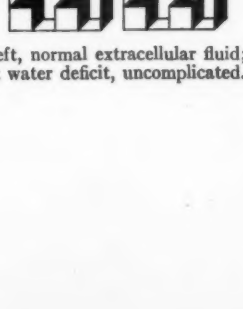

Fig. 4. At left, normal extracellular fluid; at right, extracellular salt water deficit, uncomplicated.

[1]Maximum rate of water excretion by the kidney.

[2]Hypotension of hemorrhagic, traumatic, anesthetic, cardiac, or extracellular fluid volume deficit origin, acute anoxia, obstructive jaundice, acute renal disease, etc.

[3]Water drinking is fast and renal excretion is slow following hemorrhage.

erally associated with states of water deficit or excess, or states of alkalosis or acidosis. A continued excretion of sodium in excess of that taken into the body is its cause. The excretion may be extrarenal (vomiting, diarrhea, fistulae) or renal. The renal excretion may be compensatory as in chronic water deficit or pathologic as in renal tubular hypofunction (hydronephrotic atrophy). The associated presence of water equilibrium disturbances will depend upon the concomitant rate of water accretion. If less water is drunk during the development of the extracellular salt water deficit than was lost through kidney, skin and lung, an associated deficit will be present. The development of changes in composition, alkalosis or acidosis, are mainly dependent upon the composition of the fluid lost from the body. Pyloric obstruction with vomiting of an acid solution tends to be associated with an alkalosis. Loss of pancreatic juice, an alkaline solution (pancreatic fistula), produces acidosis.

The signs and symptoms of an extracellular salt water deficit are variable. They depend in part upon the rate of formation of the deficit,[1] upon the water content of the body other than that in the extracellular fluid, upon the concomitant rate of potassium loss, and upon the degree of the "uncompensated" compositional changes that may be associated with the deficit. The signs and symptoms of a relatively uncomplicated deficit are as follows:

1. Usually there are no definite signs or symptoms associated with a salt water deficit of 0 to 2 per cent B_w in a healthy adult.[2] However, in the aged in winter and in the chronically ill, a reduction of the extracellular salt water volume of this degree may be attended by severe symptoms and signs.

2. An extracellular salt water volume decrease of 2 to 4 per cent[2] B_w is accompanied by apathy, weakness, somnolence, anorexia, brief periods of nausea, reduced affective responses,[3] transient vertigo on assuming the erect posture, a soft pulse with insignificant and variable changes in systolic blood pressure and pulse rate, and a slightly sticky skin. This stage has been called the "early barbituric-acid-depressive phase of salt deficiency."

3. An extracellular salt water volume decrease of 4 to 6 per cent B_w[4] ($1/5$ to $1/3$) of the extracellular fluid volume) is associated with an increase in severity of the above signs and symptoms and in addition: occasional unproductive retching, syncope on attempting to stand, a lowered blood pressure—frequently to "shock" levels, a variable pulse rate—usually tachycardia, a subnormal temperature if ambient temperature is below 85°F.[5], a wrinkled tongue, sticky skin, "putty" muscles, and soft eyeballs.

4. Coma finally supervenes and death occurs with reductions of the extracellular salt water volume of $1/3$ to $1/2$ of the "normal."

The laboratory signs are variable and are in part dependent upon the amount of the deficit (little change of solute concentration with small deficits regardless of rate of water ingestion) (11), upon the composition of the salt solution excreted (plasma chloride falls faster if stomach contents are lost than if small bowel contents are), upon the rate of water accretion in deficits of salt water volume greater than 2 to 3 per cent B_w (see chronic water deficit and extracellular salt water deficit with "relative" water excess), and upon the rate of development of the deficit.

The finding of "normal" blood solute or red blood cell concentrations does not rule out the presence of an extracellular salt deficit. However, a diminution of the solute concentration (Na and Cl) with an increase in the concentration of red blood cells (high hematocrit) is positive evidence that a relatively severe and rapidly developed extracellular salt water deficit exists. The relationship of the changes in solute and red blood cell concentrations to the salt water deficit are qualitative but usually not quantitative. Therefore the history and the physical examination constitute the best bases for ascertainment of the existence of salt water deficit.

[1] The more rapidly the deficit develops, the more severe are the symptoms and signs that accompany a given deficit.

[2] Author's observations on C.A.M. Three trials, fasting state for 14 hours, volume deficit induced by continuous duodenal drainage for 50 hours excepting for eight ½-hour periods with the tube clamped to permit the drinking of water to allay severe thirst.

[3] No desire to smoke, read the paper, or talk to anyone.

[4] B_w—original body weight.

[5] When extracellular salt water volume deficits are associated with a proportionately greater water deficit, when they are very great and the individual is near death, when it occurs in infancy, or when it is incurred in hot climates, an elevated temperature is usually found.

Extracellular salt water deficit with water deficit (Fig. 5). The primary cause of extracellular salt water deficit with water deficit is the loss of extracellular salt water attended by the accretion of water at a rate slower than its rate of loss through skin and lung. This state is

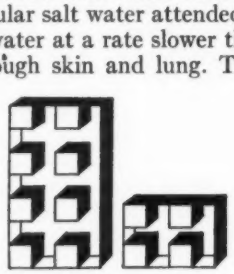

Fig. 5. At left, normal extracellular fluid; at right, extracellular salt water deficit with water deficit.

similar to chronic water deficit. However, differences exist between them. An individual suffering from a primary salt water deficit with water deficit relates a history from which a loss of sodium in vomitus, diarrhea, fistulous drainage, or sweating may be inferred; and as a rule one suffering from chronic water deficit does not. Uncompensated compositional changes in extracellular fluid, acidosis or alkalosis, are more prone to occur with primary salt water deficit with water deficit than with chronic water deficit. In the latter state the base is lost through the kidney in combination with anions (Cl, HCO_3, HPO_4, SO_4 and organic acid radicals) in proportions that tend to keep the ratio of acid to base bicarbonate within normal range. In primary salt water deficit the sodium is lost from the body in combination with different proportions of chloride and bicarbonate, and the ratio of acid to base bicarbonate will tend to vary depending upon the source of the body fluid lost. For instance, with the vomiting of pyloric obstruction in the presence of chlorhydria, more chloride is lost than sodium which results ultimately in an uncompensated alkalosis. With pancreatic fistulous drainage, more base bicarbonate than chloride is lost, and acidosis occurs. The impairment of health usually proceeds more rapidly with primary salt water deficit than with chronic water deficit.

The signs and symptoms of an extracellular salt water deficit with water deficit are a combination of those described for extracellular salt water deficit, acute water deficit, and for the compositional change that may attend. Thirst may be absent in spite of a relatively severe water deficit, presumably due to the dulling of the sensorium attendant upon the development of the salt water deficit.

The physical signs of an extracellular salt water deficiency, oliguria, an increased blood urea, a relatively normal base concentration, and variable chloride concentrations characterize this state.

Extracellular salt water deficit with relative water excess (Fig. 6). Dehydration with hypochloremia, and the hypochloremic state are relatively nondescriptive terms that have been applied to this condition. A reduction in the body content of sodium with dilution of the remaining body base by ingested or parenterally administered water is its cause. Small

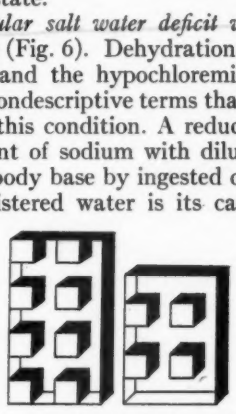

Fig. 6. At left, normal extracellular fluid; at right, extracellular salt water deficit with water excess.

deficits of body base are not attended by dilution of body solutes with water even though large volumes of water may be made available to the body, provided that the renal excretion of water is not limited by factors other than the diminution of the salt water volume (11). However, large deficits of sodium, and more especially those associated with hypotension, are associated with a dilution of the remaining body base provided that water is available to the organism at rates greater than the rate of water loss. In other words, the kidney tends to maintain a normal solute concentration in body fluids in the face of a small salt water deficit but is unable to do so when deficits of salt water become severe, if water is available to the body at a rate greater than that of loss.[1]

[1]Extracellular (salt water) deficit with relative water excess may be associated with many pathological conditions: With chronic diarrhea associated with anal stricture, incomplete obstruction of the colon, ulcerative colitis, and gastrocolic or enterocolic fistula; with persistent vomiting of incomplete pyloric stenosis, duodenal and small intestinal polypoid growths, and segmental stenosing enteritis; with the chronic loss of body fluids

Theoretically the actual water content of the body in this state, although it is usually in deficit, may actually be in excess of the individual's usual content in health even though extracellular fluid volume is below normal in spite of its dilution with water. To have this particular condition readily obtain it is necessary that the loss of extracellular sodium proceed without much reduction of intracellular base and with a rate of water accretion that is faster than its rate of loss.

A full blown picture of an extracellular salt water deficit with water intoxication does not occur often with environmental temperatures below 85 degrees F. However, at low environmental temperatures it may complicate the course of recovery from trauma (operative, 20; thermal, 22; crush) provided that too much water is given too soon or that too little sodium is given too late. The rate of excretion of positive loads of water by the kidney is reduced and may approach zero with severe salt water deficits. In oliguric or anuric states associated with an extracellular salt water deficit, the restoration of the solute volume and the concentration of the extracellular fluids by the administration of an appropriate interstitial salt solution is of primary importance in the re-establishment of kidney function. If an attempt be made to force urine flow by the administration of water before the extracellular fluid volume deficit is corrected, severe water intoxication may be induced, and an oliguria converted to anuria.

Extracellular salt water deficit with water excess (miner's cramps) occurs fairly frequently in hot environments if a sodium deficit is incurred while the drinking or the administration of water is not limited (21). Heavy work by an untrained, unacclimatized person (high rate of Na loss through sweating) and a reduction of sodium intake below minimal rate of loss in a person at rest (alcoholism, febrile illnesses, etc.) are the usual immediate causes of the sodium deficit.

through fistulous tracts (duodenal, choledochal, pancreatic and enteral); with the chronic loss of extracellular fluid from granulating wounds; and with inattention to details in the care of people with large wounds (placing individuals with large open wounds or granulating surfaces in tubs of water rather than saline, the covering of large wounds with wet dressings that are wet with water or hypotonic salt solutions as boric acid).

The physical signs and symptoms of an extracellular salt water deficit with relative water excess are those of an extracellular salt water deficit, those of an absolute water excess, and those of uncompensated compositional changes if they are present. Obviously large individual variations in signs and symptoms will be present. The laboratory signs of an extracellular salt water deficit with relative water excess are as follows: a low sum of the plasma chloride and bicarbonate (below 115 to 120 mEq. per liter) in the absence of acetonuria, a low urine chloride concentration, and a normal or an increased concentration of red blood cells. These are the most essential correlatives to be considered in formulating a diagnosis of an extracellular salt water deficit with relative water excess.

Extracellular salt water excess (Fig. 7). The symptoms and signs of a rapidly induced relatively small excess are listed in Table III. The sensible loads at the end of the period of loading varied from 2.8 to 4.1 percent of body weight because of the excretion of the salt water (renal and intestinal) that occurred during the loading period. The volume of

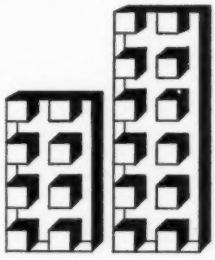

Fig. 7. At left, normal extracellular fluid; at right, extracellular salt water excess.

fluid given always amounted to 5 per cent body weight in 5 hours.

The signs and symptoms vary and seem to be partially dependent upon the composition and tonicity of the solution that was administered, especially by the oral route. Haldane and Priestley described this relationship earlier. The salt solution drunk "was meant to approximate to the salt content of human serum and was found to be much more palatable than .6 p.c. sodium chloride solution—a point of some practical importance because it

TABLE III.—SYMPTOMS AND SIGNS OF EXTRACELLULAR SALT WATER EXCESS IN MAN

Symptoms	Group 1	2	3	4
Chilly sensations	100%	100%	0%	40%
Nausea	100	20	0	0
Hoarseness	100	100	100	100
Abdominal cramps	88	20	0	0
Lethargy	66	40	100	40
Heavy eyelids	77	100	100	100
Headache	44	0	0	0
Somnolence	44	0	80	0
Thirst	66	100	100	0
Signs				
Personality changes (Irritability or depression)	77	0	40	0
Massive repeated watery stools	66	0	0	0
Minimal edema of legs	44	60	80	0
Minimal edema of hands and legs	11	20	20	0
Muscle incoordination	44	0	60	0
Dyspnea with mild exertion	0	0	80	0
Vomiting	0	0	0	0

Group 1: Nine healthy fasting men, loaded with 5 per cent B_w of 0.85 per cent NaCl solution at a rate of 1 per cent B_w per hour by mouth.

Group 2: Five healthy fasting men, loaded with 5 per cent B_w of 0.85 per cent interstitial salt solution (NaCl, 124 mEq. per liter, plus $NaHCO_3$, 30 mEq. per liter, in water) at a rate of 1 per cent B_w per hour by mouth.

Group 3: Five healthy fasting men, loaded intravenously with 5 per cent B_w of 0.85 per cent NaCl solution at a rate of 1 per cent B_w per hour (0.85% NaCl in 5% glucose solution produced more severe post-administrational muscular incoordination).

Group 4: Five healthy fasting men, loaded with 5 per cent B_w of 0.6 per cent NaCl solution at a rate of 1 per cent B_w per hour by mouth.

was found to be almost impossible to drink rapidly two or three litres of sodium chloride solution without producing vomiting" (17).

Hoarseness and a sensation of "heavy eyelids" are the only constant symptoms associated with a sensible load of 2.8 to 4.1 per cent body weight of the above solutions. Greater positive loads of salt solutions are associated with the gross collection of fluid in subcutaneous tissue, in body cavities and in some organs. Therefore, gross overloads of 15 to 25 per cent body weight are associated with variable signs and symptoms that have an intimate relationship to the degree and rate of impairment of breathing, circulation and renal function.

Extracellular salt water excess rarely exists without a disturbance in the content of water in the body in relation to total solutes. A relative water deficit is commonly associated with it. This state is described below.

Extracellular salt water excess with relative water deficit (Fig. 8). This syndrome may be readily induced during the postoperative period and after trauma by the exclusive use of an isotonic salt solution to provide for the water and salt needs of a person who cannot

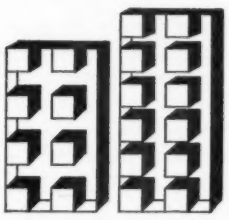

Fig. 8. At left, normal extracellular fluid; at right, extracellular salt water excess with water deficit.

eat or drink. It is physiologically analogous to the illness induced by drinking sea water to satisfy thirst.

If 0.9 per cent sodium chloride solution (159 mEq. sodium per liter) is the only fluid infused into healthy fasting men, the urine excreted during the first 24 hours does not contain much more sodium than the infusate per unit volume. Consequently, the amount of water made available to the body from the saline solution is smaller than the insensible loss of water and the concentration of salt in body fluids increases.

If the intravenous injection of 0.9 per cent sodium chloride in water or 0.9 per cent sodium chloride in 5 per cent glucose into a healthy man is continued at a constant rate during the next 24 hours so that an amount of solution roughly in excess of 3 per cent of body weight is administered in 24 hours, a new equilibrium state tends to be established. This state is characterized by the excretion of the salt given that day, and by a concentration of sodium chloride in the urine sufficiently greater than its concentration in the infusate so that enough water is thereby provided to balance the insensible loss, and the concentration of salt in the body remains at the level reached

the previous day or it decreases. If the above solutions are given as the sole source of water during renal insufficiency states or during the immediate postoperative period, when the kidneys' ability to excrete sodium in high concentrations in the urine is limited, a much greater excess of sodium chloride and a greater deficit of water in relation to total body solutes will exist before the new equilibrium state is reached. Indirect evidence indicates that under certain circumstances the relative water deficit may reach such proportions as to be associated with anuria in the presence of edema. The syndrome of "acute salt intolerance" is now thought to be due to salt excess with a relative water deficit.

The symptoms and signs are as follows: disorientation, anorexia, nausea, vomiting, a diminishing rate of urinary flow in relation to the amount of fluid retained, hoarseness, and the collection of fluid subcutaneously, in the lungs, and in body cavities. The plasma sodium concentration tends to be elevated, and the red blood cell count and plasma protein concentration tend to be reduced. If oliguria is present, the nonprotein nitrogen of blood increases.

Changes in composition of extracellular fluid. (Departure from the normal electrolytic pattern of extracellular salt water.) Changes in the composition of extracellular fluid can be of many types. A few of them are: hypoproteinemia, hyperproteinemia; hypocalcemia, hypercalcemia; hypochloremia, hyperchloremia; and acidosis, alkalosis. Only two of them, acidosis and alkalosis of nonrespiratory origin, will be considered.

The degree of acidosis or alkalosis present should be looked upon as a measure of the organism's inability to compensate for a change in the relationship of the bicarbonate ion to the anions of stronger acids (SO_4, HPO_4, Cl, lactate) in the extracellular salt water. In other words, the actual change in the hydrion concentration (acidosis or alkalosis) is a measure of the ineffectiveness of the respiration, the renal function, and the buffer systems to compensate for an alteration in the relationship of acid (H_2CO_3) to base bicarbonate ($BHCO_3$)—HA/BA. This change in relationship in the type of acidosis or alkalosis considered here is due to a shift in the proportion of $\bar{H}CO_3$ to the sum of the other anions of stronger acids than H_2CO_3 in the extracellular fluid ($\bar{C}l$, $\bar{H}PO_4$, $\bar{S}O_4$, lactic and other organic acids).

The signs and symptoms of a relatively uncomplicated[1] base-bicarbonate deficit ("acidosis") and of a base-bicarbonate excess ("alkalosis") are relatively mild. The reduction by one-half[2] of the base bicarbonate (to 10–14 mEq. per liter) by drinking hydrochloric acid is attended by moderate dyspnea and hyperpnea with mild exercise, such as walking at one's usual rate on level ground, and severe dyspnea after rapidly climbing three flights of stairs, similar to that which may be experienced during the last 50 yards of the "440." There is no appreciable dyspnea or sense of fatigue at rest, but recovery of a feeling of well-being after exercise is long delayed with the above base-bicarbonate deficit. No great change in the mental reactivity was noted at the above level of base-bicarbonate deficit. Greater noncompensatory deficits of base bicarbonate to one-quarter of normal (7–8 mEq. per liter) in adults (13) and to less than one-fifth of normal (4–5 mEq. per liter) in children (13) may not be attended by any grossly detectable signs or symptoms indicating an impairment of the function of the central nervous system.

Similarly, the elevation of base bicarbonate to 40 to 52 milliequivalents per liter of plasma (CO_2 combining capacity 90 to 120 volumes per cent) may not be associated with any detectable mental or physical signs of illness; even the tendency to the development of muscular cramps and hyperexcitability of tendon reflexes may not be apparent. Hypopnea is difficult of detection without actual measurement of the minute volume of respiration. Therefore it appears that most of the symptoms usually ascribed to "acidosis" (base-bicarbonate deficit)[3] and "alkalosis" (base-bicarbonate excess) are the result of the concomit-

[1] Acidosis—rapidly induced by drinking N/100 hydrochloric acid.

[2] Alkalosis—rapidly induced by drinking 1.25 per cent $NaHCO_3$ in water.

[3] Disorientation, anorexia, nausea, vomiting, weakness, apathy, pain in muscles, paralytic ileus, hypotension, fast pulse.

ant disturbances in physiologic components other than base bicarbonate. Fagge in 1874 (9) first called attention to the apparent rôle played by dehydration (salt water deficit) in the clinical picture of diabetic coma and to the partial efficacy of the injection of a saline solution into the blood. However, following Stadelmann's implication of acid poisoning as the cause of diabetic coma, the rôle of the salt water volume deficit in the picture of diabetic coma was largely forgotten for a time.

Within the last two decades Fagge's original ideas have been rediscovered, and it is now realized that salt water deficits (extracellular ($\overset{+}{Na} : \overset{-}{Cl}, \overset{-}{HCO_3}$) and intracellular ($\overset{+}{K} : \overset{-}{HPO_4}$)) may quite frequently accompany nonrespiratory base bicarbonate deficits and base bicarbonate excesses. Consequently, as more experience is gained in treating individuals suffering from disturbances in body-fluid equilibrium, it is realized that the symptoms and signs of severe "alkalosis" or "acidosis," with their ubiquitous physiologic effects, may be minimal; and that it should be more generally realized that the direction of one's efforts toward their correction without taking cognizance of the relatively large neutral salt water deficits that are associated with them will occasionally result in inadequate salt water replacement. Then the signs and symptoms ordinarily ascribed to the alkalosis or acidosis, excepting those related to respiration and in the case of alkalosis those relating to ionized calcium deficit, may persist though to a lesser degree after the carbon dioxide combining capacity has been returned to normal. Therefore, in the treatment of a base-bicarbonate excess or deficit the replacement of the attendant neutral salt water deficit should always be kept in mind. See Table IV for the treatment of acidosis and alkalosis.

Extracellular salt water distributional shifts (Fig. 9). (Reciprocal variations in the extracellular salt water volume of various tissues, with the total extracellular salt water volume of the body remaining constant.) This type of disturbance in fluid equilibrium is frequently seen by the surgeon. Varying degrees thereof universally accompany all trauma. The experiments of Underhill, Kapsinow, and Fiske

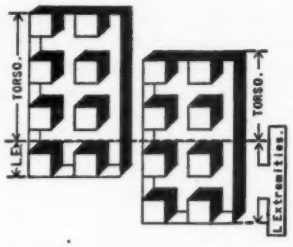

Fig. 9. Extracellular distributional shift from torso to lower extremities.

(23) demonstrated that the rate of shift of fluid into an injured area is rapid, and that after the fluid has entered the injured area, it does not leave it in appreciable amounts for 50 to 70 hours. The increment of fluid in the injured area actually constitutes a functional loss of salt water and plasma proteins from the body (the uninjured part). Red blood cells also collect in the injured tissue, largely because of the capillary dilatation and the stasic flow of blood in it. This constitutes a functional hemorrhage although the total red cell volume remains within normal limits as determined indirectly from the hematocrit and plasma volume determinations or directly using carbon monoxide.

A distributional shift of body fluids following trauma is similar to an uncomplicated extracellular salt water deficit or a chronic water deficit. Clinically significant distributional shifts of body fluids are associated with trauma (mechanical, e.g. crushing injuries, fractures of the pelvis and femora, major operative procedures; thermal, e.g. scald and burn; and chemical, e.g. peritonitis following perforation of the duodenum or gall bladder); with thrombophlebitis; with infections such as gas gangrene, typhus fever, and trichinosis; and with toxic dermatoses. This list is not complete.

Salt water (see Table IV, distributional shift), blood, and plasma protein constitute the basic therapeutic elements in the treatment of distributional shifts of body fluids.

More detailed and specific directions for the treatment of disturbances in the equilibrium of body fluids than those included in this paper can be found in the *Journal of the American Medical Association* (3) and in the *New England Journal of Medicine* (1).

TABLE IV.—TREATMENT OUTLINE

Fluid volume state	Repair solution	Concentration of solute in repair solution	Composition of repair solutions		
			Compositional change in extracellular fluid		
			Alkali normal	Alkali deficit[1] (Minimal—moderate)	Alkali excess[1] (Minimal—moderate)
Acute water deficit	Glucose in water	5, 10, or 15%			
Chronic water deficit Extracellular salt water deficit with water deficit	Sodium salts	100 mEq./liter*	Sodium chloride plus sodium bicarbonate (or lactate) plus potassium chloride. Ratio $NaCl : NaHCO_3 : KClmEq$ 4 : 1.0 : 0.166		Sodium chloride
Water excess	Sodium salts	180 to 360 mEq./liter	Sodium chloride plus sodium bicarbonate (or lactate) plus potassium chloride Ratio $NaCl : NaHCO_3 : KClmEq$ 4 : 1.0 : 0.166		Sodium chloride
Extracellular salt water deficit with relative water excess	Sodium salts	160 to 250 mEq./liter	Sodium chloride plus sodium bicarbonate (or lactate) plus potassium chloride Ratio $NaCl : NaHCO_3 : KClmEq$ 4 : 1.0 : 0.166		Sodium chloride
Extracellular salt water distributional shifts	Sodium salts	100 to 160 mEq./liter	Sodium chloride plus sodium bicarbonate (or lactate) plus potassium chloride Ratio $NaCl : NaHCO_3 : KClmEq$ 4 : 1.0 : 0.166		Sodium chloride
Extracellular salt water excess with or without a relative water deficit	Glucose in water	10 to 15%			

*Salt dissolved in water or in 5 per cent glucose solution.

[1]When disturbed fluid volume states coexist with *severe* compositional disturbances, the initial treatment should be directed toward the correction of the alkalosis or acidosis. In the treatment of alkalosis, M/100 HCl or a 0.9 per cent solution of NH_4Cl are effective. In the treatment of severe acidosis, sodium bicarbonate (1.3% solution) or sodium lactate (M/6 solution) may be used. When the signs of shock or liver damage are present, sodium bicarbonate is to be preferred to sodium lactate because the latter may not be split by the liver of a person who is very ill; and if it is not split, it is not effective in the treatment of acidosis.

The amount of acid or alkali to be employed in the initial treatment of a base-bicarbonate deficit or excess may be determined as follows:

(1) In the treatment of acidosis, use 60 mgm. of sodium bicarbonate per kilogram of body weight as a 1.3 per cent solution for each mEq. the base bicarbonate is below 25 mEq. per liter of plasma. The amount can also be obtained without calculation by the use of Van Slyke's nomogram (24). The employment of this formula to calculate the base bicarbonate needed to correct a given base-bicarbonate deficit will provide enough $NaHCO_3$ to replenish both the intracellular and extracellular deficits (5).

(2) For the initial treatment of alkalosis, employ the following rule. Take 0.063 cubic centimeter of concentrated HCl (36 per cent) per kilogram of body weight for each mEq. the base bicarbonate is above 30 mEq. per liter of plasma; dilute it with 0.9 per cent NaCl solution so that not more than 5 cubic centimeters of concentrated acid is present in 100 cubic centimeters of saline; then give it slowly and stop the injection if dyspnea appears (2).

If the necessary laboratory data are not available, changes in physical signs may be used in regulating the amount of sodium bicarbonate or hydrochloric acid to be given. In the case of severe acidosis, sodium bicarbonate solution (1.3 per cent) may be infused intravenously until the hyperpnea and the dyspnea are relieved; usually in an adult two liters of 1.3 per cent $NaHCO_3$ will be enough. With severe alkalosis, M/100 HCl or 0.9 per cent NH_4Cl may be given until the carpopedal spasm and the hypopnea are relieved.

After the initial correction of the compositional abnormality, the extracellular salt water deficit that remains is corrected with appropriate solutions. The extracellular salt water deficit associated with acidosis or alkalosis (excepting alkalosis due to the ingestion of alkali) is almost always relatively greater than the alkali excess or deficit, and therefore after the initial correction of the compositional changes, more salt solution of a relatively neutral reaction should be given to correct the extracellular salt water deficit that remains.

Therapy. The conduct of parenteral fluid therapy should be primarily determined from an evaluation of the history, the symptoms, the physical signs, and laboratory data. Laboratory data are valuable but should not be used as the primary determinants of diagnosis or procedure. Some of the reasons for the above statement follow:

a. The quantitative correlation of the departure from normal values of the hemoglobin and the hematocrit with changes in the extravascular salt water volume in experimental sodium deficiency states is poor and is negative occasionally. This is the more especially true the more slowly the salt water deficit is contracted and the longer it exists (14, 15). If hematocrit and hemoglobin changes are used as bases for the calculation of the fluid-need, an underestimation will usually be made.

b. The concentration of plasma proteins is also a "poor" constant. In many instances of known sodium salt deficit, the total circulating protein diminishes at approximately the same rate as the volumes of the plasma and the extravascular extracellular fluid do (8). Consequently, the plasma protein concentration may not be above normal even though a dangerous degree of extracellular salt water depletion may be present.

c. The plasma chloride level does not constitute a valid basis for ascertaining either the presence or the degree of change in the extracellular salt water volume. The plasma chloride concentration may not fall and may ac-

tually increase as an extracellular salt water volume deficit occurs as a result of pancreatic or biliary drainage, and it may be below normal when the extracellular fluid volume is normal (hypochloremia secondary to a primary carbon dioxide excess as in emphysema, asthma, depression of breathing by opiates) or when the extracellular salt water volume is even greater than normal (hypochloremia secondary to an excess of water as in water intoxication).

The weight of the body from day to day is not an universally sound physiologic basis for the determination of the salt and water needs of the individual. Distributional shifts of extracellular salt water into the subcutaneous tissues or into serous cavities occasionally occur rapidly, and as a result thereof the rest of the body suffers from the depletion of its extracellular salt water—there is need for salt water even though the individual's weight has not changed. Conversely, an individual who has been given salt water or plasma in the treatment of injury (burns) usually begins to lose weight rapidly between the fourth and seventh days as the edema of the burned area subsides. Salt water should not then be given to the patient even though he is losing weight because he is excreting the salt that was given to him while the edema was forming; and now that the edema is subsiding the salt constitutes an excess. If one assumes that except for the above types of illnesses, weight change is a sound basis for controlling fluid administration, he assumes that the "ideal" water and salt contents of the body are constant. This is likely not true though only a small amount of exploratory research work has been done on the possible changes in the "ideal"[1] body content of water and salt associated with various ills. Under certain circumstances the "ideal" water and salt contents of the body may be larger and under others smaller than they are in the healthy individual.

When determinations of the volumes of plasma and extracellular salt water can be made easily and repeatedly, they may become valuable aids in the diagnosis and treatment of disturbances in body-fluid equilibrium.

[1] "Ideal" contents may be defined as those most conducive to the rapid recovery of health.

Changes in the concentration of plasma solutes and red blood cells are most valuable as checks of the appropriateness of the diagnosis and treatment.

Because there are no simple dependable means of detecting small extracellular salt water deficits, the daily parenteral administration of salt to those who cannot eat or drink is presumably an expedient that should be employed even though no salt is being lost through extrarenal channels or sequestrated in diverse regions of the body. How much salt should be given under these circumstances?

Because healthy nonfasting men habitually eat 2 to 10 grams of salt daily, it has been felt that a sick man who cannot eat should receive parenterally at least 5 grams a day in order to maintain his "salt balance." However, men suffer no apparent harm if their salt intakes are reduced to 1 gram daily. The Tlascalan Indians forgot the taste and the use of salt after they had been cut off from salt for centuries (16). Infants sustain their most rapid period of growth on about a gram of sodium chloride per diem.

It appears likely that the salt that man ingests daily is dictated by taste and habit rather than by actual need, and that healthy men in general have within their bodies more salt than is actually necessary for the maintenance of health. Quantitative salt excretion studies lend support to this idea. The question of the optimal salt intake, during a fast, is still unanswered. From a surgical standpoint, the routine parenteral administration of 5 to 9 grams of salt daily when there is no abnormal functional loss thereof is in certain instances capable of delaying recovery. In fact, a *slight deficit* of extracellular salt water may be preferable to any excess (even 5 to 9 grams daily), especially during the immediate postoperative period. This belief is supported by a number of reasons:

1. For 2 to 4 days after any injury, injected salt solutions tend to collect most rapidly and to a relatively greater extent in the area of injury (19). This phenomenon is very easily demonstrated in anyone upon whom a colostomy has been performed. If no saline is given, the transudation from the surface of the loop will be relatively small and it swells

relatively little; if then 2,000 cubic centimeters of 0.9 per cent saline solution are administered, the transudation and swelling increase rapidly. An enteric anastomosis behaves in the same way; the edema that occurs about the region of the anastomosis is greater if saline is given. Therefore, the resumption of the functional continuity of the intestine following an enteroenterostomy or enterocolostomy will tend to be longer delayed as the amount of salt injected is increased. On one occasion an edematous occlusion of a gastrojejunostomy stoma was found to be the cause of a complete gastrojejunal obstruction 24 days after a subtotal gastric resection. The mass of salt given daily was 4 grams over that lost as gastric drainage. No subcutaneous edema was present. Following the second operation, although no corrective operative procedure was carried out, the functional patency of the anastomosis was established after 4 days of a zero intake of salt. The rate of healing of wounds tends to be related inversely to the local edema; the greater the edema, the slower is the rate of healing. This is most clearly demonstrated in the experiments performed by Glen, Gilbert and Drinker.

2. The incidence of postoperative pulmonary complications after upper abdominal operations is higher, especially in the aged, when maintenance doses (5 to 9 grams daily) are infused than when no salt is given unless specific signs of need appear. (Unpublished data.)

3. A deficit of extracellular salt water is more easily corrected than an excess.

The adoption of the policy of withholding salt during the immediate postoperative period until signs of its need appear shifts the responsibility for the maintenance of a physiologically adequate extracellular salt water volume from the kidneys of the patient to his physician. This responsibility is big. *If signs of illness are present or appear after an operation or injury that are attributable to a functional extracellular salt water deficit, contracted by an external loss or an internal shift thereof, vigorous saline therapy must be instituted, and the consequences of local edema forgotten.*

If there are indications for the parenteral administration of fluids, what solution or solutions should be employed? In general, the solution used should be so composed as to effect the return to normal of the various deformations of the body's fluids without producing other deformations that may be more difficult of accommodation by the organism than the original ones were. Obviously, if the kidneys of all sick individuals would perform as do those of healthy men, the manufacture of a universally applicable repair solution would be feasible; in fact, 0.9 per cent sodium chloride in water or in 5 per cent glucose (glucose-saline) could serve in that capacity.

If a water deficit existed, it could be corrected by the administration of 0.9 per cent sodium chloride in amounts in excess of 3,000 cubic centimeters daily, should the kidney excrete urine that contained 1.8 per cent salt; for then all the salt injected could be excreted in one-half the volume of water that was injected as 0.9 per cent salt, thus making available to the body a volume of water equal to the volume of urine.

If a water excess existed and the kidney excreted the sodium chloride in 0.9 per cent concentration or lower, the water content of the body would decrease by an amount equal to, or greater than, the insensible loss of water.

If alkalosis existed, the excess of chloride relative to sodium in the 0.9 per cent sodium chloride solution, compared to the concentration of chloride relative to sodium in plasma, would serve to reduce the alkalosis (the concentration of alkali) even should the kidneys put out no urine. If acidosis was present, the administration of 0.9 per cent sodium chloride would permit its correction if the kidneys were capable of excreting sufficiently greater amounts of chloride than sodium.

However, the kidneys of men and women who have been injured or operated upon are relatively unable to excrete a urine having a higher concentration of sodium chloride in it than is present in 0.9 per cent sodium chloride, and consequently water deficits tend to be increased rather than alleviated by the administration of 0.9 per cent sodium chloride solution. In addition, the kidney's ability to excrete chloride in excess of sodium is reduced following trauma or an operation, and therefore the correction of an acidosis with sodium chloride may be impossible.

In other words, solutions of 0.9 per cent sodium chloride in water or in 5 per cent glucose (glucose-saline) are not universally applicable repair solutions because the renal function tends to be depressed following operations and trauma. Therefore, the solutions employed in the correction of fluid disequilibrium states should be so constituted as to effect the correction without depending upon the kidneys.

The solutions that fit the physiologic requirement for the correction of the fluid disequilibrium states described herein are listed in Table IV.

The volume of fluid administered and the rate of administration depend largely upon the response of the individual and the constitutional severity of the depletion.[1] Usually the volume of salt solution given in 24 hours should not exceed 6 per cent of the weight of the body unless the rate of functional loss of extracellular salt water continues at a rapid rate, either as a result of the continuance of distributional shifts (burns, trauma, peritonitis, gas gangrene) or as a result of continued high rates of external loss (ileostomy, colostomy, or other fistulous drainage). Under these latter conditions the infusion of salt water may have to be continued to 10 to 15 per cent of the weight of the body per 24 hours. When a rapid rate of infusion is employed or a large volume of fluid is given, repeated auscultation of the chest and gross determination of venous pressure should be performed. If râles appear, or if the veins of the neck become distended and tense, the infusion should be temporarily discontinued.

After the correction of deficits has been effected, the amount of salt water given daily will depend upon the continued existence of the cause of the deficit. If the cause of the deficit is a distributional shift, due to an injury, the movement of extracellular fluid into the injured part will tend to decrease rapidly so that after 36 hours there will be little further shift. After 72 to 100 (23) hours have elapsed after the injury, the extracellular fluid in the injured part will begin moving back into the rest of the body, and no more salt should be given because a functional excess of extracellular salt water then exists. If the loss of extracellular salt water continues (because of hyposthenuric nephropathy, fistulous drainage, diarrhea, vomiting, gastroduodenal drainage) the loss of salt should be made up, as it occurs, by the injection of a saline solution that has the salt compositional pattern of the body fluid lost.[2] (See Gamble for the composition of various body fluids.) If no salt is lost after the correction of the deficit, very little if any need be given.

Another general physiologic principle that should be kept in mind when one prescribes parenteral fluids is: A primary change in the body's content of one substance is associated with changes in the organism's content of other substances; consequently, the restitution to normal of the primary change in content does not insure the restitution to normal of the secondary changes upon which the ultimate recovery of the person may rest. For example; a man, who excretes large amounts of hydrochloric acid into his stomach, develops pyloric obstruction and vomits; a large amount of chloride and a smaller amount of sodium are lost in the vomitus. This increases the concentration of base-bicarbonate in the body and the *p*H of the extracellular fluid increases; respiration slows and the amount of carbon dioxide in the body increases, base-bicarbonate is excreted through the kidney, and the body's content of base, and consequently of extracellular salt water, are thereby diminished. Sodium enters the cells of the body (6) and potassium leaves them to be excreted; a deficit of potassium is incurred thereby. The volumes of plasma and of extravascular extracellular salt water decrease, plasma protein leaves the blood stream (8), and the total circulating protein falls although none is lost externally. The red cell mass actually declines although the hematocrit may rise (14).

Now let the extracellular salt water volume deficit be replaced by the infusion of 0.9 per

[1]Men with extracellular salt water depletion associated with signs of "shock" receive more solution at a faster rate than those having extracellular salt water depletion without signs of "shock."

[2]Sweat, give NaCl 0.45 to 0.6 per cent; gastric drainage with free hydrochloric acid in it, give NaCl 0.45 to 0.6 per cent; hyposthenuric nephropathy and enterostomy drainage (ileostomy or long-tube suction), give NaCl plus $NaHCO_3$ plus KCl (see Table IV); pancreatic fistula, give osmotically equivalent masses of NaCl plus $NaHCO_3$ (3 grams NaCl plus 4 grams $NaHCO_3$ per liter).

cent sodium chloride solution; the chloride and sodium deficits and a part of the carbon dioxide and base-bicarbonate excesses are relieved. There still exists a deficit of plasma protein, a deficit of red blood cells, and an intracellular potassium deficit and sodium excess. (The chemical signs of an intracellular potassium deficit are: a persistently high carbon dioxide combining capacity, a high blood urea (or non protein nitrogen), and a low chloride concentration in plasma [4].) If an attempt is made to "correct" the high carbon dioxide combining power and the "hypochloremia" by further administration of sodium chloride, the deficit of potassium tends to be aggravated regardless of whether the sodium chloride is retained or excreted, and the chloride concentration of plasma remains low and the carbon dioxide combining power high.

Therefore, it is obvious that the infusion of sodium salts alone will not satisfy the physiologic demands of the organism after reconstitution of the extracellular salt water volume, and that the transfusion of whole blood and the administration of potassium salts should be considered as integral parts of the treatment of a large salt water deficit (7) especially if it has developed slowly and is associated with pronounced physical signs such as great weakness, atonic muscles, and hypotension. Upon theoretical (10) and clinical grounds the transfusion of blood should be withheld until partial reconstitution of the extracellular volume has been effected, in order to minimize the tendency for the intravascular agglutination of red blood cells and clotting. Darrow (4 to 7) has demonstrated recently that a deficit of potassium frequently accompanies disturbances of extracellular fluid equilibrium, and that it has great physiologic and clinical significance.

SUMMARY

A clinical plan is presented for the recognition of disturbances in the equilibrium of body fluids.

The disturbances in equilibrium considered are: (1) acute water deficit; (2) chronic water deficit; (3) absolute water excess; (4) extracellular salt water deficit, uncomplicated; (5) extracellular salt water deficit with water deficit; (6) extracellular salt water deficit with water excess; (7) extracellular salt water excess; (8) extracellular salt water excess with water deficit; (9) changes in composition of extracellular fluids (electrolytic pattern); (10) distributional shifts of extracellular salt water.

The general principles of therapy involved are:

1. It is better to treat the man than it is to treat his "blood chemistry," plasma proteins, hematocrit, or weight. A presumptive clinical understanding of the types of disturbances in the equilibrium of body fluids may be gained from a correlation of the history and the physical examination of the patient. The laboratory data are valuable as checks of the diagnosis and treatment, but they should not be used as primary bases for either.

2. Sodium salts should be given when they are needed and should be withheld when they are not.

3. A primary change in one physiologic variable, such as the sodium content of the body, is attended by secondary changes in other physiologic variables; consequently, the restitution of the primary variable to "normal" content does not insure the return to normal of the secondary variables upon which ultimate recovery may rest. Decreases in the volume of circulating red blood cells and plasma proteins and in the mass of intracellular potassium are important secondary variables associated with sodium deficiency, especially if the sodium deficit has developed slowly.

4. The kidneys of patients treated by the surgeon are often not "alert" enough to alter a 0.9 per cent solution of sodium chloride to fit the need of the organism; therefore, appropriately balanced salt solutions should be used.

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USE OF BLOOD AND BLOOD SUBSTITUTES

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IN recent years much new information regarding the nature, origin, and function of different elements of the blood has become available through the researches of biochemists, physicists, physiologists and clinicians. In many instances the clinical applicability of such information has been obvious and the patient has derived immediate benefit. In this field as elsewhere in medicine progress in the care of the sick depends not only on the fundamental contributions from laboratories of basic science but on the clinician's alert and intelligent appraisal of new facts and on his skilful application of these new facts in the clinic.

Whipple and his collaborators have done much to define the facts of protein metabolism and the conditions governing the regeneration of the plasma proteins and hemoglobin (10, 14, 15). The quality and quantity of protein ingested, the state of the liver, the presence or absence of infection or intoxications, the factor of individual organismal variation, and the availability of iron to the body have been shown to be critical conditions in the maintenance of normal hemoglobin and plasma protein concentrations and blood volume. They have shown that the healthy animal, for example, can replace all its circulating plasma protein in 3 days under the stimulus of plasma withdrawal while taking a protein-rich diet. Hemoglobin, which contributes six times as much protein to the blood as does plasma protein, takes about six times as long for replacement. Body protein accretion (both new hemoglobin and tissue protein) is believed to go through the transition stage of plasma protein. The protein of the plasma thus constitutes a pool which is drawn upon by the cells throughout the body and which is in constant interchange with cell protein. The studies of Schoenheimer and others using tagged elements supports the conception of continual and rapid movement of amino acids throughout the proteins of the body. The blood, then, must be regarded as a tissue which is in dynamic equilibrium with the other tissues of the body, and its composition and volume are maintained relatively constant only through a set of remarkably complex and continuous reactions.

Of particular interest to surgeons also is the work of Cohn and his group in the fractionation and characterization of the plasma proteins (3, 4, 9). As methods have been developed for the separation of the different proteins of the plasma it has become possible to prepare them for tests of their function, with a consequent better understanding of the physiological rôle of the individual proteins. The properties of the different fractions are of great clinical import, and must be considered in the intelligent use of blood and blood substitutes. For example, the colloid osmotic force of plasma proteins is essential to the maintenance of the volume of the circulating blood, and when the plasma protein concentration falls below a so-called critical level, in the neighborhood of 5 grams per 100 cubic centimeters, reduction in blood volume and dangerous tissue edema may occur. It must be remembered, however, that the albumin fraction is much more important than the globulin fraction in this respect, for although the albumin molecule comprises only about 60 per cent of the plasma protein it is a much smaller molecule than globulin and provides about 80 per cent of the colloid osmotic pressure of the plasma. It has been shown that the antibody properties of the plasma reside in the globulin component, and reduction in this fraction by malnutrition, prolonged abnormal loss, or impairment of the body's power to form globulin lowers resistance to infection (2). The clotting power of the blood depends particularly on two components of the plasma protein, namely, fibrin-

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ogen and the globulin prothrombin. In addition, an antihemophiliac globulin has been isolated and this element, missing in hemophilia, can be supplied from normal plasma to control the bleeding of hemophilia. Largely through the work of Cohn and his group, under the stimulus of war-time needs, these various derivatives of the plasma proteins have been put to practical test for the benefit of the sick and the wounded.

These remarks serve as a reminder that in the use of blood and blood substitutes in surgical practice one is dealing with fundamental physiological considerations. The better the understanding of the need of the patient, the clearer the objectives, and the less empirical the practice, the better the result.

The rest of this discussion will be concerned with two common surgical problems, namely, hemorrhage and secondary shock. These conditions will be considered in relation to therapy by the intravenous administration of whole blood, plasma, albumin solution, and protein hydrolysates. By the latter term is meant the mixture of polypeptides and amino acids formed by the enzymatic breakdown of a high quality protein such as casein or lactalbumin. Such hydrolysates in 5 or 10 per cent solution are nonallergenic and nonpyrogenic when properly prepared. They may be regarded as a blood substitute in that they provide the essential amino acids for the construction of plasma protein and hemoglobin when given intravenously.

Hemorrhage. In the healthy adult the volume of the blood comprises about 8 per cent of body weight, but variations of from 6 to 10 per cent have been found in different individuals (8, 18). The blood volume tends to remain constant in the same individual and is probably more closely related to surface area and height than to weight. The healthy person can withstand a sudden loss of one-third the blood, or even more (up to 1.5 or 2 liters), but this is not true of many of the patients the surgeon must treat. Malnutrition, previous hemorrhage, infection, trauma, disease of cardiovascular system, liver or kidneys, reduce the power of the organism to make the life-saving adjustments required in overcoming critical blood loss.

As previously noted the blood volume is not to be regarded as a fixed entity, as if contained in a rigid-walled vessel. Not only may the size of the vascular bed vary rapidly through vasodilatation, or vasoconstriction and ischemic shunts, but the blood is in diffusion equilibrium with the larger reservoirs of interstitial and intracellular fluid. With loss of blood an immediate inflow of fluid from outside the capillary bed begins, a process which is detectable by fall in red cell count and hematocrit. Furthermore, in hemorrhage protein is mobilized from parenchymatous organs such as the liver and red cells are drawn into circulation from the spleen and bone marrow. The more rapid the loss of blood, the less the time for successful compensation; and the lower the physiological reserve of the patient the smaller his capacity to endure hemorrhage. It has been shown by studies of hemorrhagic shock in animals that the longer hemorrhagic hypotension and tissue anoxia are allowed to go uncorrected the less the likelihood of survival. After a certain point damage to such organs as the liver and brain becomes progressive. The urgent need for correction of blood loss is thus emphasized. Ideally the loss of blood should be made good as it takes place.

A great service has been done practicing surgeons by Coller and his co-workers, as well as others, in providing evidence that the amount of blood lost during common operations in good hands may be large (1, 5, 6, 7, 12, 20). Many surgeons unquestionably had failed to appreciate that operative and postoperative shock commonly stemmed from uncorrected hemorrhage. Further proof is convincingly available in the major teaching clinics of the country today, where by the free use of blood transfusion during and after operation surgical procedures of hitherto impossible magnitude are being successfully performed (13). As Coller has pointed out, (a) the amount of bleeding at operation is almost always greater than the surgeon suspects; (b) there is no practicable method of measuring the extent to which bleeding has occurred at any given time during operation; and (c) replacement is most effective when whole blood is given as the loss occurs (5). Every

surgeon undertaking major surgical procedures should familiarize himself with the range of values for blood loss at various operations, and ideally he should measure the losses at his own hands in a series of cases.

The replacement therapy for massive hemorrhage seems obvious, though from time to time the obvious has been held suspect. Whole blood has been lost in the operative field, into body cavities, into tissue planes, or to the surface, and whole blood should be given in treatment (11, 19). The blood must be carefully matched, it must be given in large enough quantity, it must be given without delay. The acutely depleted blood volume, lowered cardiac output and tissue anoxia urgently require relief. In acute hemorrhage, plasma or albumin injected intravenously will increase blood volume, but further dilution of hemoglobin and crippling of the mechanism for oxygen-carriage results. Under these circumstances the systolic blood pressure may temporarily rise and produce a false sense of security while the patient's condition is actually worse.

Following a severe nonfatal hemorrhage, unless the loss has been completely corrected by blood transfusion, a period ensues during which anemia, hypoproteinemia, and reduced blood volume are common findings. Unless the patient is receiving large amounts of iron the anemia is apt to be of the hypochromic microcytic type, and the hypoproteinemia may be associated with a relatively greater reduction of albumin than of globulin. During the convalescence from severe hemorrhage further blood transfusions are still frequently in order, but protein requirements may be advantageously contributed to by infusions of plasma and albumin. A better source, however, of amino acids is protein hydrolysate in 5 or 10 per cent solution.

Secondary shock. In the state of secondary shock as distinct from neurogenic, transitory hypotension there are present reduction in cardiac output and blood flow, fall in blood pressure, and usually evidence of peripheral arteriolar constriction. As a rule there is lowered basal metabolic rate and body temperature, rapid pulse, shallow respiration, and sweating. Secondary shock may be seen in medical as well as surgical conditions and the syndrome may be classified on an etiological basis as follows:

1. Loss of propulsive force, or cardiogenic shock as seen in coronary occlusion and severe cardiac arrhythmias.

2. Dilatation of the vascular bed, as seen in overwhelming invasive infections or in transection of the spinal cord.

3. Mechanical interference with blood flow, as in volvulus of the intestine, cardiac tamponade, tension pneumothorax, pulmonary embolism, or mesenteric thrombosis.

4. Primary reduction in blood volume, as in wound shock, hemorrhage, burns, war-gas poisoning and severe dehydration.

The classification of secondary shock in this manner is of value in that it emphasizes the varied nature of forces which may produce the same clinical picture, though in many cases more than one of these major causes may be at work. It follows that treatment will vary likewise.

It is probably a fair assumption that reduction in cardiac output is present in secondary shock due to any of the above causes, and that lowered blood volume is present in most instances. However, blood transfusion may be dangerous rather than beneficial in cardiogenic shock or pulmonary embolism, and though blood transfusion is helpful in intestinal strangulation it is equally important to correct the mechanical defect by early surgical operation. In the state of secondary shock due to fulminating infections, restoration of blood volume by infusions of plasma and by blood transfusions is in order, but of greater urgency perhaps is treatment of the infection itself, as by surgical operation, antibiotics and sulfonamides depending on the case (17). The uncritical use of blood transfusion in secondary shock without analysis of its cause is therefore to be condemned.

In the state of secondary shock due to losses from the circulation, or in other words in primary oligemic shock, successful treatment must be based on knowledge of the nature of the losses. In wound shock, including the shock incident to surgical operation, oligemia is due to loss of whole blood, and the treatment that is needed is blood transfusion in suf-

ficient volume. Furthermore, the treatment of such cases of hemorrhagic oligemia does not end with recovery from the hypotension, as was pointed out above. Incomplete restoration of lost blood, the presence of complicating infection, the wasting effect of the "reaction of injury" raise the need for protein. The intravenous route must often be employed in meeting this need, and 5 or 10 per cent amino acids solutions, plasma, albumin, and whole blood must be given.

To illustrate the need for discrimination further, the parenteral fluid requirements in wound shock and in burn shock may be compared. In both conditions there is severe reduction in the volume of circulating blood. In wound shock, however, whole blood has been lost, and the hematocrit and red cell count are normal or low, the plasma protein concentration is normal or low. In burn shock, plasma has been lost in large amounts, and albumin frequently to a greater extent than globulin; the hematocrit and red cell count are sharply elevated. Correction of blood composition here is important as well as restoration of blood volume, and the immediate intravenous therapy of choice is infusion of plasma or albumin solution. In both wound shock and burn shock blood and protein hydrolysates and to a less extent plasma and albumin solution may be required intravenously in later convalescence.

CONCLUSIONS

In conclusion certain general principles involved in the use of blood and blood substitutes in the treatment of hemorrhage and shock are listed:

1. Careful matching of blood before transfusion is essential in minimizing reactions and renal damage; plasma for infusion should be of the pooled mixed variety or it should be typed.

2. Deficiency of hemoglobin and deficiency of plasma protein often occur together, whether the lack is acute or chronic.

3. In the restoration of depleted blood volume by intravenous injections normal blood composition as well as normal volume should be the aim.

4. Acute losses of hemoglobin are less easily repaired by the body than are losses of plasma protein.

5. In infections, toxic states and trauma regeneration of hemoglobin and plasma protein may be greatly impaired.

6. The longer tissue anoxia due to hemorrhage and shock is allowed to go uncorrected the less the likelihood that the patient will recover.

7. In hemorrhage and shock as seen in surgical patients the need for blood transfusion and for infusions of protein and the protein derivatives often continues during convalescence.

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LIGATION OF THE INFERIOR VENA CAVA IN THROMBOSIS OF THE DEEP VEINS OF THE LOWER EXTREMITIES

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LIGATION of the major veins to limit propagation of blood clots and prevent pulmonary embolism has become a standard procedure. The point of ligation of the involved vein depends upon the level of the blood clot and the extent of disease of the vein. The only safe rule to follow is to ligate above the clot through a normal segment of vein just below a main tributary. The majority of cases of thrombosis of the veins of the lower extremity can be detected while the clot is still below the inguinal ligament. In these, ligation of the femoral vein for the deep venous thrombosis, and the saphenous vein for superficial thrombosis, usually terminates the process. However, in some the disease has extended to such a level that ligation of the inferior vena cava becomes necessary. Ligation of the inferior vena cava is not a new procedure. It has been quite widely used in pelvic thrombophlebitis. However, it has only recently been used to any extent in the treatment of thrombosis of the deep veins of the lower extremities. We have performed ligation of the inferior vena cava in 30 cases of ascending thrombosis of the deep veins of the lower extremities. A report of these cases forms the basis for this communication.

INDICATIONS FOR LIGATION OF INFERIOR VENA CAVA

Although the indications for ligation of the inferior vena cava were essentially the same in all of our cases, the basic venous pathology was quite varied (Chart 1). In this series there were 3 types of venous thrombosis, namely, phlebothrombosis, acute femoroiliac thrombophlebitis, and thrombophlebitis in varicose veins (Table I). The relative dangers of pulmonary embolism in the various types and the necessity for ligation of the inferior vena cava in the cases we are reporting can best be shown by description of the pathology and clinical course of each type.

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PHLEBOTHROMBOSIS

Phlebothrombosis usually begins in the small veins of the legs or feet. The clot is attached at first only at its origin. Propagation is the characteristic quality of this type of venous thrombosis. As the original mass of clot begins to organize, the vein wall at this level becomes thickened, edematous, and inflamed. As new clot is added it extends steadily upward floating freely in the blood stream. The clot gradually fills the involved veins and eventually becomes organized and fixed to the vein wall. This process may require many weeks. Until there is complete organization and fixation of the thrombus it may be dislodged at any time and produce pulmonary embolism. Phlebothrombosis is particularly dangerous because at first there may be no local symptoms. Its existence often becomes known only after the patient has suffered one or more episodes of pulmonary embolism. As the clot extends upward more venous channels become occluded and local signs and symptoms develop. In all of the cases in this series there were local signs and symptoms of venous thrombosis. The common signs are edema of the foot, ankle, and leg; dilated superficial veins; cyanosis of the nail beds; and often a fall in local temperature. Pain in the calf is the most important symptom. This may be constant but is more often noted on motion of the foot or leg or on pressure over the veins. Fever is frequently absent and when present is quite mild. Leucocytosis is usually absent.

Phlebothrombosis of the deep veins of the legs accounted for 25 of the cases in this series.

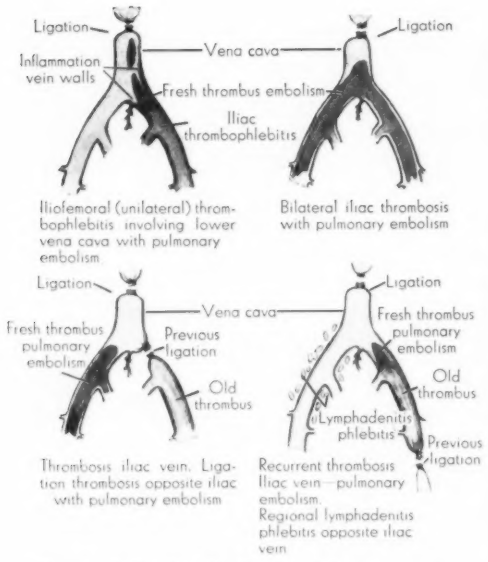

Chart 1. Indications for ligation of the vena cava.

In 21 the process involved both legs and in 4 only one leg. In all the disease had extended above the inguinal ligament on one or both sides. In 4 cases a previous ligation of one or more veins at lower level had failed to check the process and recurrent pulmonary embolism ensued. In 15 the blood clotting started after a period of bed rest, 7 in medical cases and 8 in surgical patients. In 10 the disease occurred in apparently healthy and normally active people. The ages varied from 38 to 73 years. There were 15 males and 10 females. In this group of 25 cases 23 had had one or more episodes of pulmonary embolism before ligation of the inferior vena cava. There were no instances of embolism following ligation. There were 3 deaths in this group. Two deaths occurred in cardiac patients and one died of pneumonia (Table II).

ACUTE FEMOROILIAC THROMBOPHLEBITIS

Acute femoroiliac thrombophlebitis begins with inflammation of the vein wall. Blood clot forms on the inflamed intima and is firmly attached from the beginning. The clot is usually confined to the segment of inflamed veins. Because of the fixation and limitation of the

TABLE I.—TYPES OF THROMBOSIS

	Cases	Pulmonary embolism
Phlebothrombosis—deep veins (Bilateral 21—Unilateral 4)	25	23
Acute femoroiliac thrombophlebitis	3	3
Thrombophlebitis in varicose veins	2	2
Total	30	28

thrombus pulmonary embolism is rare. The signs and symptoms of acute femoroiliac thrombophlebitis are usually well defined and the diagnosis is quite clear. The disease is usually ushered in with pain and tenderness in the femoroiliac region. Fever is constant and ranges up to 105 degrees F. and is accompanied by leucocytosis. The pain involves not only the region of the inflamed veins but the entire limb. It is often referred to the hip and lateral aspect of the upper thigh. The pain may be constant but is aggravated by motion of the limb. Swelling rapidly ensues after complete occlusion of the vein by the thrombus. There are usually signs of vasospasm, at least early in the course of the disease. During this acute stage embolism is very rare. As organization develops occasionally fresh clot forms on the proximal portion and may propagate into a higher segment and may become dislodged. Such emboli are usually large and may prove fatal. If not fatal one may expect a subsequent episode.

In the 3 of our cases of femoroiliac thrombophlebitis which required vena caval ligation the course of events were somewhat similar. In all, the patients were young, 24, 30, 31 years. In each the process involved the left extremity and seemed to have reached a safe period. In one, 2 weeks had elapsed between onset of the disease and occurrence of the first embolus. There was a quiescent period of 4 and 5 weeks respectively in the second and third cases before pulmonary embolism. In all 3 cases exploration of the left iliac vein re-

TABLE II.—

Predisposing causes	No. cases	Average age	Died
Bed rest—medical diseases—cardiac, 6; pneumonia, 1	7	64	3
Bed rest—surgical diseases—Abdominal, 6; fractures, 2	8	54	0
Spontaneous—normal activities	10	48	0
Total	25		3

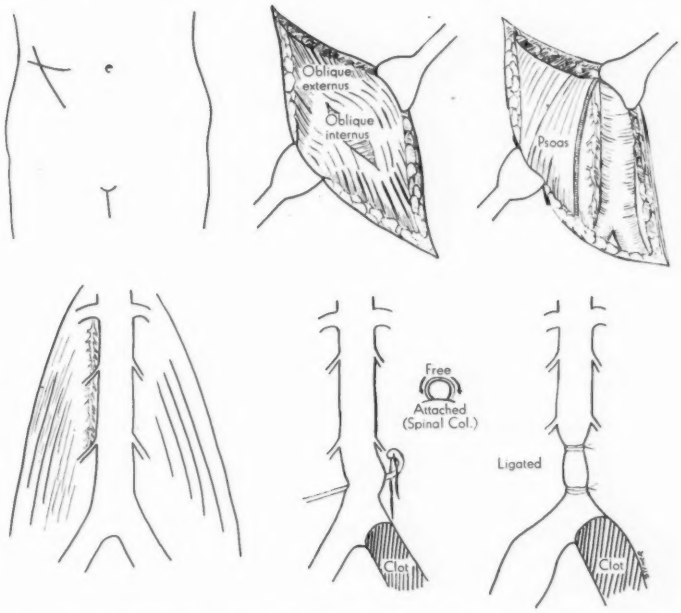

Chart 2. Diagrammatic sketches illustrating the retroperitoneal approach and ligation of the inferior vena cava.

vealed that the disease process had extended completely to the vena cava and a clot was projecting into it. Ligation of inferior vena cava was imperative (Table III).

THROMBOPHLEBITIS IN VARICOSE VEINS

One of the most common complications of varicose veins is acute thrombosis of a segment of the dilated vein. The thrombosis may follow direct trauma but more often occurs spontaneously. Usually there is a definite inflammatory reaction in the vein wall and surrounding tissue. The clot forms on the intima in the inflamed vein and is attached at that level. However, the clot spreads upward and often downward. The propagating clot at first is not attached and may project into a deep vein. As the clot spreads the vein wall becomes inflamed and the clot adheres to the intima. The inflammation and clot may spread to the femoral vein and eventually produce thrombophlebitis in this vein. The projecting clot may be dislodged and produce pulmonary embolism. In 2 of our cases such a sequence of events did occur. In both there was at first a localized area of thrombophlebitis in a segment of varicose veins. This process slowly spread through the entire great saphenous veins and into the femorals. In one the saphenous veins were ligated but the disease had already spread to the femoral veins. Subsequently both femoral veins became occluded and the patient began to have episodes of pulmonary embolism. In the other the course was similar except that the saphenous veins were not ligated. At the time of our exploration both iliac veins in each case were thrombosed and the disease could be checked only by ligation of the inferior vena cava.

TECHNIQUE OF OPERATION

The inferior vena cava can be readily exposed by a retroperitoneal approach. The in-

TABLE III.—

Predisposing causes	No. cases	Average age	Died
Post-partal	2	27	0
Postoperative	1	31	0
Varicose veins	2	48	0

TABLE IV.—

	Cases	Early reaction	Late reaction
Preoperative bilateral deep vein thrombosis.....	24	0	24 Edema
Preoperative unilateral deep vein thrombosis....	6	2	6 Edema
Immediate congestion—vasospasm and massive edema—relieved by sympathetic block, 2 cases			
All six unilateral cases developed thrombosis in opposite leg			

cision, preferably transverse, is made on the right side at the level of the umbilicus. It begins at the lateral margin of the rectus and extends laterally into the flank. It should be about 6 inches in length. First the incision extends through the skin and subcutaneous fat down to the external oblique muscle and fascia. This muscle is then split in the direction of its fibers for about 6 inches. This exposes the internal oblique muscle which in turn is split in the direction of its fibers. The transversus abdominis muscle then comes into view. It is split in the direction of its fibers and the entire opening is enlarged to admit wide exploration. At this level one can explore the lower vena cava, the right common iliac and palpate the upper portion of the left common iliac vein. As the transversus abdominis muscle is opened the retroperitoneal fat bulges into the incision. This is reflected medially and the iliopsoas muscle is identified. By further retraction of the retroperitoneal tissue the ureter and vena cava are exposed. The vena cava is quite mobile except posteriorly where it is attached loosely over the vertebrae. The vena cava is inspected and palpated. It should be blue—and easily compressed. Occasionally enlarged lymph glands partially cover it and these must be carefully dissected. After exposure the vena cava is gently elevated from its bed, great care being used to prevent tearing small branches. When the vessel has been completely freed a curved ligature carrier threaded with No. 8 cotton thread is passed around it and the ligature tied firmly. A second ligature is placed about ½ inch higher. We have not found it necessary to explore the veins unless the wall is thickened and one cannot be sure a clot is not present. The incision is closed in the usual manner (Chart 2).

LOCAL CIRCULATORY CHANGES FOLLOWING LIGATION OF THE INFERIOR VENA CAVA

The local vascular changes following ligation of the inferior vena cava depends upon the extent of the thrombosis already present in the deep veins. In our cases the thrombosis was extensive, and had lasted for some days. In 24 cases the deep veins of both legs were involved and the process had extended into the iliac veins. In 6 cases the venous pathology was confined to one extremity. There was usually some edema of the involved parts, as well as a variable degree of venous congestion. So many of the cases had had varicose veins before onset of their disease that a comparative study seemed useless. In some there was a mild degree of arterial spasm. In the 24 cases of bilateral thrombosis there was practically no demonstrable changes immediately following operation. In the 6 unilateral cases, however, the vascular reaction was profound. Two of these demand a detailed description (Table IV).

In one, immediately upon completion of the operation there was severe congestion of the normal limb. There was extreme pain and the limb became blue, mottled, and cold. The pulse of the tibial arteries and popliteal artery disappeared. A sympathetic block (1% novocain) promptly administered caused the pain to subside. The color rapidly returned to the normal pink, and the pulse could be felt again in the leg and foot. The limb was elevated some 18 inches. There was no further acute discomfort, but the deep veins became thrombosed and diffuse superficial collateral veins developed rapidly.

The second case in which severe circulatory disturbance developed presented somewhat a milder picture. There was no immediate congestion. Some 8 hours after ligation the patient experienced a severe generalized pain in normal leg. The leg began to swell, became cyanotic, cold, and the pulses of the leg disappeared. Shortly after onset of the symptoms a lumbar sympathetic block was performed. The pain subsided but there were less changes in color and temperature. Eventually 8 sym-

pathetic blocks were performed over a 3 day period before there was relief of symptoms. The deep veins became thrombosed, and superficial collaterals developed rapidly.

The remaining 4 unilateral cases all developed thrombosis of the deep veins of the normal side with massive edema of that limb. The process was gradual and at no time was there any disturbance of the arterial circulation. In all of our 30 cases there has been some degree of postoperative edema of both legs. This has been controlled by properly fitted elastic stockings. We have used a series of leg exercises in order to expand the collateral circulation gradually (Chart 3). The legs are elevated on 4 soft pillows immediately after operation. Walking motion exercises of the feet and legs are given frequently. As the edema subsides, or if negligible throughout, the pillows are gradually lowered. About 10 days following operation the patients are allowed to dangle legs over the side of the bed—still using the exercises. About 14 days after the operation the patients are allowed to walk. Elastic stockings are then fitted and are worn at all times except while in bed. The patient gradually resumes free activity. All of the patients that survived have been rehabilitated to the point of resuming full time occupations. There has been no ulceration of the legs. There is a marked difference in the rapidity of development of collaterals in the males and females. In the males the superficial collaterals have predominated; in the females the deep collaterals, and often there is no dilatation of the superficial veins.

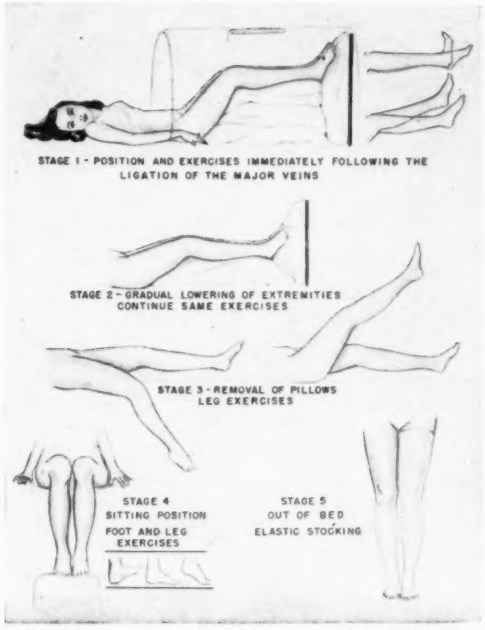
STAGE 1 - POSITION AND EXERCISES IMMEDIATELY FOLLOWING THE LIGATION OF THE MAJOR VEINS
STAGE 2 - GRADUAL LOWERING OF EXTREMITIES CONTINUE SAME EXERCISES
STAGE 3 - REMOVAL OF PILLOWS LEG EXERCISES
STAGE 4 SITTING POSITION FOOT AND LEG EXERCISES
STAGE 5 OUT OF BED ELASTIC STOCKING

Chart 3. Postoperative measures to restore venous circulation.

VENOUS COLLATERAL PATHWAYS FOLLOWING LIGATION OF THE INFERIOR VENA CAVA

When the inferior vena cava is ligated many collateral pathways develop. Some of these carry blood back to the inferior vena cava above the point of ligation, others communicate with the portal vein or the superior vena caval system. Among the most important deep collateral routes is the communication of the hypogastric vein with the inferior mesenteric vein through the hemorrhoidal plexus. Another major route is from the external iliac vein through the inferior epigastric vein to the superior mesenteric vein and thence to the superior vena caval system. In women an additional important deep pathway is found in the ovarian veins which have access to blood from the hypogastric veins through the pelvic and uterine plexuses and deliver it to the inferior vena cava directly or via the renal vein. In men the homologous pathway through the spermatic veins is considerably less efficient, which probably explains the clinical observation that the superficial abdominal veins usually are more prominent in men than in women after ligation of the inferior vena cava. The main superficial collateral circulation is from the femoral vein through the superficial epigastric vein to reach the superior vena caval system by communication with the lateral thoracic vein. Other veins which contribute to the collateral circulation include the vertebral venous system (communication through pelvic plexuses), the lumbar veins (communication through the deep iliac circumflex vein and iliolumbar vein), and the superficial iliac circumflex and superficial internal circumflex branches of the femoral vein.

SUMMARY

Ligation of inferior vena cava is indicated in ascending thrombosis of the lower extremities, with pulmonary embolism, when the diseased process has reached above the inguinal ligament. The extraperitoneal approach is best suited for ligation of the inferior vena cava in such cases. Phlebothrombosis is most likely to produce pulmonary embolism. We have presented 30 cases of ligation of the inferior vena cava, 25 of which were due to phlebothrombosis, 3 femoroiliac thrombophlebitis, and 2 to thrombophlebitis in varicose veins.

There were 28 instances of pulmonary embolism before ligation of the inferior vena cava. There were none following ligation. There were 3 deaths, 2 in cardiac patients, and one pneumonia.

There has been adequate development of collateral venous circulation in all of those who survived. Women develop better venous collaterals than men.

NUTRITIONAL PREPARATION FOR SUBSTANDARD RISK PATIENTS

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THE number of publications which have appeared during the war years and since, attest to the current interest among investigators and clinicians, in nutritional problems. As a consequence of these efforts, it is now possible to list better methods for solving the dilemma of the surgeon contemplating a major operation on a patient who is a substandard risk as a result of a chronic dietary deficiency. When, from unhappy personal experiences, surgeons had learned to calculate the added risks these individuals suffered, often, in the past, a number were denied benefits obtainable through surgery; or, if accepted after a genuine appraisal of the increased hazard, the necessary surgical manipulations were found to be poorly tolerated. The patient seemed to react unfavorably from the outset, with an instability of blood pressure, out of proportion to the actual blood loss. Blood transfusions would often produce only a transient and unsatisfactory response. Frequently, the convalescence was protracted; complications developed to jeopardize the patient's life. In a considerable number, a vitality sufficient to meet all the requirements for convalescence was so lacking that death occurred despite recourse to a variety of therapeutic measures. The usual autopsy findings of some incipient heart failure and bronchopneumonia, a fatty liver, or a failure of wound healing, were hardly an exoneration, but rather confirmed the impression that malnourished individuals presented a substandard risk. Too frequently the issue will continue to be settled tragically if surgeons persist merely in restoring to normal the hydration, electrolyte status, and hemoglobin content. The statement has facetiously been offered that some modern surgeons find it necessary to operate by the calendar while others can "work by the clock." However, a measure of wisdom may well be with the former when dealing with chronically starved patients, because an increased experience with the preoperative phase of dietary preparation indicates that the success of an operation may hinge on the effectiveness of such nutritional care, and makes unnecessary the completion of a hasty dissection before the patient's condition deteriorates. Such a statement implies that the pathologic biochemical states resulting from starvation are reversible after an appropriate dietary regimen. In nearly all except premortem instances this is possible. The rate at which the lost body protein can be replaced is much slower, though, than when balancing anew the body electrolytes or fluids. Sudden dramatic results which capture the attention are not the rule. The processes of nutritional restitution frequently require days, may even take weeks, and therefore demand of the surgeon, patience. In this regard there is a real need, as yet unanswered, for simple, accurate methods of determining how seriously starved the patient actually is; how much nourishment, and how long, should he be fed before an operation can be undertaken without an added risk. Fortunately, however, a partial restoration of the bodily stores usually suffices to permit performance of the necessary operative procedure. That is to say, all the fat need not be forced from the liver; nor all depleted tissues refabricated; nor the hypoproteinemia completely corrected; or the immune globulins and phagocytic values restored to normalcy. Even though short of this goal, after a reasonable period of satisfactory preoperative food intake, the surgeon can then anticipate a convalescence virtually as free of complications as that encountered among the standard risk group. A discussion of the meth-

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ods and nutrients employed upon the surgical service at the University of Minnesota Hospitals, for realizing this, represents the subject matter of this paper. It is hoped that the therapeutic outline offered will prove to have a broad practical application to the several nutritional problems faced by surgeons; and by virtue of its relative inexpensiveness, simplicity of preparation, and apparent effectiveness, merit trial in the preoperative dietary preparation of surgical patients.

FACTORS RELATED TO LIQUID DIETS FORTIFIED WITH PROTEIN AND CARBOHYDRATES

During semistarvation or starvation periods, man, just as any experimental animal, becomes autocannibalistic, while deriving his energy from body fat and protein. This means that his diet necessarily is low in calories, carbohydrates, and protein, but relatively high in fat. From this one might predict that a diet of opposite qualities, namely, high in protein, carbohydrates and caloric content, would be best suited to correcting those abnormalities ascribable to this starvation regimen. The results of numerous investigations and clinical experience have confirmed this impression.

Of these several constituents, experience and experimentation have demonstrated that protein plays a chief rôle. The principal sources of protein in natural foods are meat, fish, eggs, certain dairy products, and cereals. Yet, in each of these, the protein contributes but a fraction of the total bulk. It, therefore, becomes necessary to consume relatively enormous quantities of food when very high protein diets are desired. For example, to realize an intake of 300 grams of protein from beef, a pot roast between 3 and 4 pounds would have to be eaten. This is a feat usually beyond the capacity of any individual weakened and apathetic from prolonged starvation, and is an impossibility in the case of those patients with stenosis or obstruction due to a lesion at the pyloric outlet. Desirable as it may be to foster the consumption of a high protein diet by pleasant appearing, tastily prepared menus, the physical factors indicated above limit the accomplishments possible by this means. In order to pyramid the intake from such means, liquid dietary supplements fortified with a protein concentrate and ordinarily also a carbohydrate can be used. A variety of protein concentrates are at present available, and among these is skim milk powder with the following composition:

Components	Per cent
Protein	37.8
Casein	32.0
Lactalbumin	5.2
Lactoglobulin	0.5
Carbohydrate (lactose)	49.7
Fat	1.0
Water	3.0
Ash	8.5

An experience has been acquired with use of this fortifying substance in diets prepared for treating several hundred malnourished surgical patients on the surgical service of the University of Minnesota Hospitals. Skim milk powder has a low cost, is readily and widely available in quantity, stores well in the bulk, and can be fairly well disguised in a variety of palatable mixtures. The proteins present are complete, possess a medium capacity to induce plasma protein regeneration under experimental conditions, and are rich in the liver protecting amino acid methionine. In addition, much of our biologic information on nutrition has been acquired using those proteins present in skim milk powder. They have repeatedly proved excellent sources when fed in quantity.

The use of a liquid diet either as a supplement to the hospital fare or as the sole source of calories finds frequent and valuable application in the care of patients with surgical lesions of the esophagus, stomach, and duodenum. A tale of recent weight loss can usually be found written in their admission history. This is particularly true when mild or serious degrees of obstruction are an associated complication of the disease process. Here, not uncommonly, the oft repeated acceptance of an incompletely masticated bolus of solid food leads to an insoluble problem in aboral transport and results in an even greater degree of obstruction and retention. Yet, it has not been unusual to note that when the lumen has been freed of these chunks by repeated washings, very satisfactory volumes of a liquid diet are accepted daily with little or no retention.

The fluid character of these liquid mixtures has an appeal for the dietetic staff burdened by a number of requests for special trays. Untrained workers can be easily instructed to perform the simple compoundings involved in the preparation of these formulas. Too, the use of liquid diets with a fixed caloric value has made relatively easy and practical the measurement, calculation, and charting of the daily caloric intake on the same sheet with temperature, pulse, and respiration. Nutrition is thus brought into focus at the bedside whenever chart rounds are being held. This method of day to day contact with the problem, and an accounting of the progress made or lost, is of fundamental importance for the consistently satisfactory care of those classified as substandard risks by virtue of malnourishment. Several diets have been tried but the following, with some variations, has appeared most adaptable:

DIET II

Carbohydrates		408.8 gm.	
Protein		120.4 gm.	
Fat		37.2 gm.	
Calories		2,446.0	
Volume	about	1,500.0 c.c.	
Caloric equivalent	about	1.6	
	CHO	P.	F.
6 whole eggs		36.0	36.0
2 egg whites		8.0	
4 oz. skimmed milk powder	58.8	40.4	1.2
300 gm. lactose*	300.0		
1000 gm. skim milk	50.0	36.0	
5 gr. salt (may be added when indicated)			
	408.8	120.4	37.2

*Beet, cane sugar, or cerelose can be substituted.

This mixture passes readily through an indwelling nasal tube. It can therefore be employed as a drip feeding mixture in an apparatus similar to that in Figure 1. This is employed when caring for persons so enfeebled by their disease and starvation that it is impossible for them to make the efforts necessary to get adequate amounts of food from bedside trays. For this setup it has proved advantageous to use an intravenous flask with a dependent air vent. This permits the entering bubbles, as they rise, to agitate gently the mixture and hence reduces the tendency to plugging through sedimentation. A Murphy drip apparatus is inserted into the connecting tubing, and flow rates are thus visualized and regulated by a thumb screw attachment.

Fig. 1. Drip feeding apparatus.

Most patients, however, are able to drink the mixture, and, as it is, the taste is similar to that of an eggnog. It can, of course, be flavored to suit the individual desire with chocolate, cocoa, vanilla, or other disguising substances. Some such variation is frequently employed by out-patients undergoing dietary preparation. These patients can obtain skim milk powder by prescription from the bulk stock in the drug room. Simple mimeographed directions about preparation, volume to be consumed daily, and the refrigeration requirements are given to them during the course of the out-patient workup. A brief explanation to this group, of the importance to them of this dietary preparation, usually suffices to insure their co-operation. Preparation from the out-patient approach is frequently possible except in the case of the very debilitated, and hence reduces the actual period of hospitalization in many instances to about that for the more standard risk group. Whenever this liquid diet constitutes the sole source of food for the patient, he is urged to take, if possible, about 5000 calories, i.e., 3 liters daily. In the absence of obstruction this is no great problem and the consumption of quantities greater than this is not unusual. If the diet is used as a supplement, the acceptance of even a liter adds materially to the protein and caloric intake for that day. Diarrhea has been a problem sporadically. It usually can be avoided

TABLE I. PREOPERATIVE NITROGEN BALANCE STUDY

E. E., Univ. Hosp. No. 764398, aged 59 years; diagnosis, carcinoma of stomach—150 pound weight loss

Date	URINE								STOOL	INTAKE					BLOOD						
	Vol. c.c.	Sp. gr.	Tot. N_2 gm.	Urea N_2 gm.	Amino acid N_2 gm.	Creatinine mgm.	Ammonia N_2 gm.	Sugar gm.	Total N_2 gm.	Caloric intake	Nitrogen intake gm.	Fluid intake c.c.	Weight lbs.	Weight kgm.	Total Protein gm./100c.c.	Alb. gm./100c.c.	Blob. gm./100c.c.	Urea N_2 mgm. %	Uric acid mgm. %	Nacl mgm. %	Vol. liters
4-12-46	1680	1.022	12.56	6.8	0.47	10.2	0.59	7.3		2002	0	3100	189	85.9							
4-13-46	1640	1.010	7.3	3.9	0.1	7.1	0.35	1.8		1930	0	3500	191	86.8	4.38	2.15	2.23	12.8	4.5		
4-14-46	2140	1.012	7.5	2.5	0.0	7.7	0.47	7.9		1930	0	3400									
4-15-46	2280	1.005	6.7	2.2	0.103	6.3	0.51	2.0		1930	0	3450			4.31	2.10	2.20	11.0	3.24		
		Total	34.06					Total	1.78												
	Av.	Daily	8.51				Av.	Daily	.44												
											I.V. 150 gm. Amigen										
4-16-46	2470	1.010	14.3	6.6	0.395	8.4	0.34	5.1		2367	18	4250									
4-17-46	1880	1.017	18.1	7.3	0.27	8.5	0.40	4.2		2080	18	4000	191	86.8							
4-18-46	1550	1.013	15.43	5.6	0.18	8.1	0.36	4.2		1460	18	3600	193	87.7	4.28	2.04	2.24	14	3.35		
4-19-46	1880	1.018	14.86	6.0	0.29	7.7	0.40	5.7		2080	18	4000	195	88.6							
4-20-46	1990	1.020	17.9	7.1	0.26	7.9	1.25	0.5		2080	18	4000	197	89.5							
4-21-46	1430	1.020	16.12	5.7	0.20	7.2	0.97	0.3		1488	18	4000									
		Total	96.71					Total	6.04		Total 108.0										
	Av.	Daily	16.12				Av.	Daily	1.01		Av. Daily 18.0										
4-22-46	1350	1.020	8.6	4.5	0.2	6.14	0.58	1.7		1296	0	2400	200	90.9	4.16	1.93	2.23	12.5	4.3		
4-23-46	1015	1.012	4.37	2.5	0.1	4.26	0.35	1.12		1296	0	2600	203	92.3							
								Total	6.12												
								Av.	Daily .81												

TABLE I. PREOPERATIVE NITROGEN BALANCE STUDY—Continued

E. E., Univ. Hosp. No. 764398, aged 59 years; diagnosis, carcinoma of stomach—150 pound weight loss

Date	URINE								STOOL	INTAKE						BLOOD						
	Vol. c.c.	Sp. gr.	Tot. N_2 gm.	Urea N_2 gm.	Amino acid N_2-gm.	Creatinine mgm.	Ammonia N_2 gm.	Sugar gm.	Total N_2 gm.	Caloric intake	Nitrogen intake gm.		Fluid intake c.c.	Weight lbs.	Weight kgm.	Total Protein gm./100c.c.	Alb. gm./100c.c.	Blob. gm./100c.c.	Urea N_2 mgm. %	Uric acid mgm. %	Nacl mgm. %	Vol. liters
											Amigen I.V.	Blood I.V.										
4-24-46	2470	1.017	15.29	10.1	0.4	7.9	0.42	4.62		1842	18	14.15	4000		91.1	4.22	1.95	2.27	11.0	3.5		5.5
4-25-46	2100	1.017	17.1	7.9	0.34	7.9	0.44	4.3		1696	18	14.0	4000		91.6							
4-26-46	1550	1.018	11.4	4.4	0.22	5.4	0.40	3.2		1746	18	13.3	3700		93.0							
4-27-46	1010	1.018	9.8	3.94	0.12	6.5	0.16	2.5		1650	18	14.8	4200		93.0							
		Total	53.59					Total	2.44	Total 128.25												
	Av. Daily		13.39				Av. Daily		0.61	Av. Daily 32.06												
4-28-46	840	1.015	9.22	3.2	0.13	4.2	0.126	2.5		1677	18	4.63	4600		92.7							
4-29-46	485	1.027	5.83	1.89	0.08	4.21	0.136	1.82		1425	18	4.81	4250		96.1	4.43	2.62	18.1		19		
		Total	15.05					Total	2.08	Total 45.44												
	Av. Daily		7.52				Av. Daily		1.04	Av. Daily 22.72												
4-30-46	810	1.018	9.88	2.9	0.13	5.99	0.58	1.98		0			600		98						492	
											U. Hosp. Diet #2—orally											
5-1-46	510	1.015	6.8	1.9	0.09	3.77	0.13	1.76	2.18	2300	17.08		3000		96.8	5.02	2.76	2.26	20.8		520	5.7
5-2-46	445	1.015	5.88	1.8	0.046	2.89	0.329	1.18	13.68*	1979	13.31		2850		96.1							
5-3-46	215	1.018	2.86	1.6	0.022	1.44	0.047	.679	3.28	3336	24.00		2700		97.3						600	
5-4-46	1940	1.006	10.18	6.2	0.11	4.27	0.423	1.78	6.65	2588	17.9		2350		97.0							
5-5-46	2220	1.011	8.06	5.8	0.08	4.22	0.35	1.15	6.12	2072	12.0		1400		93.2							
		Total	33.78					Total	31.91	Total 84.29												
	Av. Daily		6.76				Av. Daily		6.38	Av. Daily 16.86												

*Severe diarrhea on this day and frequent stools the last two days of the study probably raised the fecal nitrogen value.
Diet described in text.

through the maintenance of appropriate refrigeration of all portions of the diet other than the patient's immediate requirements and by the routine use of thoroughly cleansed or sterilized dispensing equipment. Should it occur despite attention to these precautions, modest doses of paregoric and amphogel will ordinarily correct the situation. Patients with ulcerative colitis or regional enteritis are rather consistent exceptions to this, however, and may develop an aggravatingly persistent diarrhea. The use of this mixture therefore is best avoided, or limited to small quantities while testing the patient's tolerance.

As indicated earlier, satisfactory objective measurements of the accomplishments of a refeeding regimen are virtually nonexistent. By trial and error methods, it has been possible to arrive at estimates of how long a patient should receive a caloric intake augmented to about 4000 or more calories daily. From experiences with several hundred nutritional problems the conclusion has been reached that if 5 to 7 days are devoted to such dietary preparation for each 10 per cent of the body weight lost, the individual will consistently be able to tolerate extensive surgical procedures. These values are admittedly empirical, and probably maximal rather than minimal. Until more critical tests are available, however, the present method offers a reasonably reliable means for calculating the duration of the special dietary regimen.

REASONS FOR DIETARY PREPARATION PREOPERATIVELY

It will be noted that emphasis has been placed upon preparation being preoperative. This appears to be an important consideration, because the weight of evidence at this time indicates a greater retention of nitrogen ingested during this phase rather than after an operation. Data from a number of laboratories (2, 4, 7, 10) as well as ours (11) confirm the accelerated loss and difficulty of securing a favorable balance of nitrogen in the recovery phase after surgery. In addition, such difficulties are pyramided when the patient, after an intestinal operation, is unable to take nourishment for several days because of ileus, nausea, or vomiting.

OTHER SOURCES OF PROTEIN AVAILABLE FOR SUPPLEMENTING DIETS

Besides skim milk powder, various substances are available as fortifying materials. The data of Madden and Whipple (6) suggest a number of possibilities. Two of these, homogenized raw pork liver and powdered bovine plasma protein, have been tested and each demonstrated (12, 13) to be definitely superior to skim milk powder for the production of protein. Unfortunately, the possibility of controlling brucellosis appears too real to permit routine use of the former. The latter so far has been obtainable only in quantities sufficient for investigational purposes despite the fact that countless tons are potentially available in the blood now sold as fertilizer or stock feed. Whereas, estimates of manufacturing costs are high when calculated on the amounts available from a few pilot plants, the application of modern production methods on a larger scale would likely result in price reductions sufficient to permit its less restricted usage. The incentive to develop the manufacturing of this product by the packing industry necessarily will await a more generalized medical recognition of, and demand for, just such a superior dietary protein. In a similar fashion a large portion of the protein of fresh caught tuna, mackerel, and sardines, is lost to human consumption (3). This, under current commercial practices, inedible fraction can be separated from its unpalatable characteristics and in this purified form possesses high biological value for hemoglobin and plasma protein formation. These tests, limited to date to small animals, might profitably be extended to clinical material. Yeast has received somewhat limited attention as a source of protein for humans due to its rather low content of sulphur containing amino acids and because of an objectionable odor and taste, which are quite difficult to disguise. These several drawbacks have been virtually eliminated in products recently developed from new strains (9). The result is a powder virtually free of unpleasant aromatic or gustatory characteristics, with as much as a 70 to 80 per cent protein content. Its effectiveness as a dietary supplement for man remains unmeasured. These, to mention but a few, con-

tributions of biochemists to general nutritional problems offer a partial solution of the search for more, better and cheaper proteins with high biological activity. Their trial in the management of clinical dietary problems assuredly seems warranted if the progress of our knowledge in this field is to parallel that in the laboratory. From the selection of materials now available for fortifying diets, broad scope is offered to the investigator in developing those combinations achieving the greatest effectiveness, with the least cost, and with the best palatability.

METHODS FOR PARENTERAL NUTRITIONAL PREPARATION

In certain nutritional problem cases, fortunately a rather small percentage, the oral route is not available for protein and caloric repletion. On a surgical service this most often results from an obstructive lesion of the esophagus, stomach, or duodenum which will ultimately require a surgical procedure of magnitude. In this situation the surgeon has essentially two alternatives. For one, he can elect to make a jejunostomy for alimentation. My personal experience with this operation has been a limited, but rather consistently unsatisfactory, one. Despite the employment of a wide variety of mixtures, severe diarrhea has invariably appeared before the quantity of material being fed reached a desirable level. The attainment of a substantial nitrogen and caloric balance under these circumstances is of course unlikely. Even when this complication has been less troublesome, convalescence has lagged. This may be related to the well documented temporary inability to anabolize protein that exists after a traumatic episode, and which has been carefully studied by several workers *vide supra*. The other alternative is the establishment of a parenteral feeding program for the dual purpose of meeting the patient's current caloric needs, and securing the maximal nitrogen retention possible under the circumstances. To this end, a daily carbohydrate intake of 200 to 250 grams is realized through the use of 10 to 20 per cent glucose solutions intravenously and isotonic glucose solutions subcutaneously. Unless this much sugar is available to the body for energy requirements, quantities either of the body proteins or of infused nitrogenous compounds continue to be catabolized for fuel. The magnitude of the carbohydrate intake therefore bears an indirect but quite essential relationship to the state of the nitrogen balance. Direct control of the state of the nitrogen balance, however, is regulated by the kind and amount of nitrogenous compounds injected. A portion of these requirements can be provided by protein hydrolysates or pure amino acid mixtures (5). The latter has not been available so far in this clinic. Several definite limitations exist with the use of the former. Between 15 and 20 hours are required to complete the infusion of six thousand cubic centimeters of 5 per cent each of the protein hydrolysate amigen and of glucose. This is about the maximum quantity acceptable in each 24 hours. If this casein hydrolysate is injected at rates much faster than this, or in greater concentrations, unpleasant systemic manifestations in our experience become more frequent. The nitrogen content of this considerable volume of fluid is theoretically equivalent to 225 grams of protein. In some cases with a long history of extreme privation and continuing rapid loss of protein (burns, massive ulceration, etc.) this quantity of nitrogen would scarcely suffice if the entire amount were available for useful metabolic activity. Actually, however, in several experiments it has been demonstrated that the total nitrogen content of a 24 hour urine collection after a venoclysis of this type contains considerably more waste nitrogen than that obtained while feeding equivalent amounts of skim milk powder or powdered bovine plasma protein. There are at least two reasonable explanations for these findings. Since differences in biological activity have been demonstrated for proteins from various sources, a material superior in all around qualities to casein (i.e., bovine plasma protein) might provide a more utilizable hydrolysate, if it were tried as the substrate. Or, the hydrolysis, by other than intestinal mechanisms, of these substances might lead to a decrease in the acceptability of the end products, perhaps through an incompleteness of processing. The salt content of amigen is of little consequence when only small

volumes are being employed but attains real significance (9 grams in 6000 cubic centimeters of 5 per cent solution) when large volumes are in use. This item becomes even more important in the presence of the hypoalbuminemia frequently present in just this type of patient. States of overhydration due to such liberal administrations of salt, and serious enough to require temporary cessation of this therapy have been noted.

This listing of these limitations should not be construed to mean that the intravenous administration of protein hydrolysates is fruitless, for no one can seriously contend but that it has an important rôle in nitrogen replacement therapy. Rather, it is hoped that the recapitulation of such inherent defects will bring their existence to the attention of those who have not so far appreciated them. Fortunately, the number of cases wholly dependent on parenteral feeding is in a minority. Such patients must be blessed with the services of conscientious house officer or interne because they demand of him and themselves an abundant patience and tact during the tedious hours of prolonged intravenous therapy. Without actually achieving the goal of large scale plasma protein regeneration those benefits which result from the employment of hydrolysates are certainly real and definitely worthwhile. Through their agency it is possible to halt or retard the steady protein losses from starvation and allied depleting mechanisms (ulceration, infection, hemorrhage). The nitrogen intake can also be augmented considerably by daily transfusions of plasma or whole blood. Although the total amount of nitrogen in a plasma or whole blood transfusion would be relatively small considered as dietary or hydrolysate nitrogen, it is proportionately more valuable because a significantly smaller fraction is lost in the urine the 24 hours after administration. This situation is particularly true when comparison is made with hydrolysate nitrogen. In this connection it appears only fair, when calculating the cost of such replacement therapy, to base one's ultimate conclusions on the amount of nitrogen the body actually retains and has available for functional purposes, rather than considering solely the price of each intravenous flask and its contents. The use of whole blood and plasma, particularly when the latter is from a pooled source, is assuredly not an unmixed blessing. The possibility of inoculating the recipient with the virus of infectious hepatitis has been emphasized recently (1, 8) and attention called to this serious hazard.

A nitrogen balance study by my associate, Dr. Arnold Kremen, and myself yields data illustrating some of the problems and limitations of parenteral alimentation discussed earlier. The final 5 day period of this study is probably a significant example of the body's greater inclination to accept and retain nitrogen when supplied orally rather than intravenously. As has been indicated, the surgeon will find a knowledge of nutrition a means of improving his care of those patients suffering from a recent serious weight loss. Failure to recognize this obligation and meet the augmented nutritional requirements of this group will be followed by an increase in the morbidity and mortality statistics. To avoid these complications, liquid diets augmented with protein rich materials are recommended whenever the oral route is available. For those patients requiring parenteral feeding, a specific program, albeit a less satisfactory one, is offered.

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COMPLETE OCCLUSION OF THE ABDOMINAL AORTA

Report of Two Patients Diagnosed by Aortography

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IN 2 patients with complete aortic block just below the origin of the renal arteries diagnoses were made during life by direct translumbar aortic injection of radiopaque medium. In 1 patient, the diagnosis was confirmed by 2 subsequent aortograms, while the other was proved at necropsy. The technique used has been described (8, 10).

CASE REPORTS

Case 1. T. H., a white man, aged 43 years, was admitted to Jefferson Hospital on February 8, 1945, with the chief complaint of pain in both ankles. He had been well until October, 1944, at which time he began to experience progressively increasing weakness of both legs, with easy fatigability and pain behind the knees on effort.

On December 7, 1944, while eating supper, he had a violent periumbilical pain, so severe that he became doubled up and broke out in a cold sweat. The pain remained localized to the periumbilical area, lasted for 1 hour, and was followed by a dull ache which persisted for several days. He was admitted to another hospital. The gastric analysis was normal, and x-ray study of the upper gastrointestinal tract revealed a small deformity at pyloric end of stomach, suggestive but not conclusive of a small ulcer.

While in the hospital, 5 days after the first acute episode of pain, he experienced a sudden attack of excruciating pain which first involved his right foot, leg, and thigh, then spread upward to the lower abdomen and finally down the other leg. The attack, which lasted about 30 minutes, was accompanied by numbness, paralysis, and extreme pallor of both lower extremities. The severe pain then subsided to a dull ache, and localized in both ankles. Sensation and motor power returned promptly.

Following discharge from the hospital, the patient experienced an almost constant ache in both ankles. The pain usually prevented sleep, and necessitated sitting on the edge of the bed with his feet resting on a chair. At the time of admission to Jefferson Hospital he could not take more than 20 steps without experiencing pain in the calves.

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One feature of the occupational history of possible importance was his employment in a cold storage room from 1941 to 1943, during which time he was intermittently exposed to low temperatures.

The patient was thin, weighed 135 pounds and appeared 50 years old. The temperature, pulse, and respirations were normal. Blood pressure was unobtainable in the lower extremities, but in the left arm was 170/120, and in the right arm 160/120. Eyegrounds showed diffuse arteriolar constriction with increased tortuosity, several pinpoint hemorrhages, and one large hemorrhage in the extreme periphery of the left eye ground. The remainder of the examination of the head, as well as the neck and chest, was essentially normal. The abdomen was normal except for the fact that aortic pulsations could not be palpated. Arterial pulsations, including the femoral, popliteal, posterior tibial, and dorsalis pedis, were not palpable in either lower extremity. Both feet were cold, the left colder than right.

The erythrocyte count was 4,400,000, hemoglobin 87 per cent, leucocytes 7,400 with normal differential count, and platelets 194,000. The blood sedimentation rate was normal. Results of repeated urine tests were normal. The blood Wassermann and Kahn reactions were negative. The blood sugar, urea nitrogen, uric acid, and serum proteins were normal. The urea clearance test was 105 per cent. The prothrombin time was 100 per cent, and tests of venous clotting time in both arms and both legs revealed hypercoagulability of the blood. Venous pressure in the upper extremities, as well as circulation time, performed by the calcium gluconate method, were normal. The electrocardiogram showed a prominent *Q*-wave in leads II and III, suggesting coronary artery disease, posterior in type.

Roentgenograms of the chest, abdomen, and spine were essentially normal. Soft tissue examination of the lower extremities failed to show any evidence of calcification in the blood vessels. Study of the upper gastrointestinal tract with barium revealed thickened mucosal folds and slight distortion of the duodenal bulb, suggestive of an old healed duodenal ulcer, and the barium enema was normal.

Circulatory function tests in the lower extremities all indicated markedly impaired function. Skin surface temperature studies failed to show an appreciable rise after paravertebral lumbar sympathetic nerve block. Peritoneoscopy revealed no evidence of an abdominal mass as a source of extrinsic aortic pressure. The left internal iliac artery and vein were

Fig. 1. First aortogram in Case 1, showing complete transverse block of abdominal aorta at level of middle of second lumbar vertebra.

Fig. 2. Second aortogram in Case 1, 2 months later, showing opaque medium within superior mesenteric artery and its branches. Arrow indicates large anastomotic communication between middle colic artery of the superior mesenteric and left colic branch of inferior mesenteric artery.

clearly visualized, but no arterial pulsation was noted. A neurosurgical consultant reported normal neurologic findings and advised that lumbar sympathectomy would be of questionable value.

Massive obstruction in the iliac arteries and the aorta itself was thought the most likely possibility, but coarctation of the aorta was also considered. It was felt that aortography might definitely prove the diagnosis. Accordingly, this procedure was first performed on February 24, 1945, with aortic puncture at the level of the upper border of the first lumbar vertebra. The arteriogram revealed a complete transverse block of the aorta at the level of the middle of the second lumbar vertebra, immediately below the origin of both renal arteries (Fig. 1). The renal arteries and their tributaries were well visualized and appeared normal. In order to rule out any errors in technique, repeat aortography was performed on April 30, 1945, puncture being made one vertebral level lower, at the upper border of the second lumbar vertebra. On this aortogram (Fig. 2), practically all of the radiopaque medium was visualized within the superior mesenteric artery and its branches, and no portion of the aorta itself was definitely delineated. Anastomosis of the middle colic branch of the superior mesenteric artery with the left colic branch of the inferior mesenteric was well demonstrated on this examination. Since the second aortogram merely confirmed the findings of the first one by inference rather than actual demonstration of the block, the study was performed for the third time on June 4, 1945. The needle was introduced at the level of the second lumbar vertebra just above the area of anticipated block. This aortogram (Fig. 3) left no doubt as to the existence of the block, which was sharply delineated at precisely the same level as on the first examination. The large anastomotic channel between the superior and inferior mesenteric arteries was again visualized, as well as an extensive paravertebral anastomosis.

Treatment and subsequent course. Anticoagulation therapy with dicoumarol, vasodilator drugs (papaverine and niacinamide; sodium citrate and sodium tetrathionate intravenously; and mecholyl by iontophoresis), and the oscillating bed were employed during his 6½ months in the hospital. One month after admission the patient developed an ischemic ulcer on the lateral aspect of the right leg just above the external malleolus (Fig. 4a). Despite the use of penicillin systemically, various local applications including blood ointment, and the measures already mentioned to improve the arterial circulation in his lower extremities, the ulcer remained refractory throughout his hospital stay. He

Fig. 3. Third aortogram in Case 1, 3 months after first aortography, showing sharp delineation of the block just below the origin of the renal arteries. An extensive paravertebral anastomosis is demonstrated.

was discharged on August 22, 1945. At this time he could walk about 50 steps before experiencing pain in the calves, and he was also able to sleep most of the night without pain in the ankles.

Three months after the patient left the hospital his leg ulcer healed (Fig. 4b), after having been present for 8 months. Follow-up examination was last performed on November 26, 1946, a year and 3 months after discharge. At this time the patient stated he felt well, could walk three city blocks without having to stop because of pain, and could do light work. Blood pressure in the left arm was 210/150, in the right arm 200/150, but unobtainable in the lower extremities. Aortic pulsation could not be detected and arterial pulsations in the lower extremities were still not palpable.

CASE 2. J. D, a white man, aged 52 years, was admitted to Jefferson Hospital on February 19, 1945, with the chief complaint of frontal headaches. These headaches, which first started in December, 1942, occurred when the patient arose in the morning and became progressively worse during the day. They could be relieved by rest and salicylate medication. In January, 1943, he was informed by a physician that he had albuminuria and a systolic blood pressure of 260. Despite treatment by doctor, he had almost daily frontal headaches, with occasional dizziness.

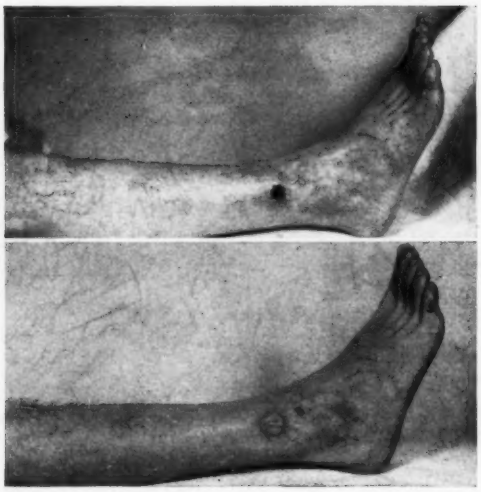

Fig. 4. Photograph, (a, above), shows ischemic ulcer of leg in Case 1, with complete healing, (b), 8 months later.

During the preceding 10 years the patient had experienced numbness, tingling, and weakness of the lower extremities particularly after prolonged effort, but never any pain. He was treated for pneumococcic lobar pneumonia in February, 1943, in another hospital. The family history was not significant.

The patient was a middle-aged thin man, weighing 118 pounds, lying comfortably in bed. The temperature, pulse, and respirations were normal. Blood pressure in the left arm was 250/130; right arm, 210/130; left thigh, 124/100; and right thigh, 130/108. Ophthalmoscopic examination revealed diffuse hypertensive retinitis with arteriosclerosis, grade 3. The remainder of the examination of the head, as well as the neck and lung fields were essentially normal. The heart was regular in rate, force, and rhythm: slightly enlarged to the left; and there were low-grade systolic murmurs at all the valve areas. There was a palpable aortic impulse in the epigastrium over which a systolic murmur was audible, but no pulsations could be detected below this area. The remainder of the abdominal examination was normal. Examination of the extremities revealed a full strong radial pulse, but arterial pulsations, including femoral, in the lower extremities were almost imperceptible.

The blood count revealed the hemoglobin to be 98 per cent, erythrocytes 5,000,000, and leucocytes 9,800 with normal differential count. The blood sedimentation rate was not increased. The blood Wassermann and Kahn reactions were negative. Repeated urinalyses revealed moderate albuminuria. The highest urine specific gravity was 1.008. The urea clearance test was 64 per cent and the phenolsulfonephthalein dye test revealed 25 per cent

Fig. 5. Aortogram in Case 2, showing complete block at precisely the same level as in Case 1. Arrow indicates huge anastomotic channel between middle colic and left colic arteries as in Figure 2.

renal excretion in one-half hour. The blood urea nitrogen was 20 milligrams. The venous pressure in the arm was 115 millimeters and the circulation time 12 seconds. The electrocardiogram suggested coronary artery insufficiency, anterior in type.

A roentgenogram of the chest revealed emphysematous lung fields, and a cardiac silhouette within normal limits. There was no notching of the ribs as might be expected with aortic coarctation. X-rays of abdomen and intravenous urogram were normal.

In spite of complete bed rest, sedation, and salt-poor diet the patient showed no improvement. Even with sodium amytal narcosis there was no appreciable decrease in hypertension. On March 7, 1945, the patient signed his own release. It was felt that the probable diagnosis was coarctation of the aorta.

The patient was readmitted on March 22, 1945, with the same complaints. The physical examination revealed no significant changes since the last admission. Blood pressure in the left arm was 236/130; right arm, 190/110; left thigh, 130/90; and the right thigh, 120/90. The blood count and urinalysis revealed essentially the same findings as before. The sedimentation rate was still normal. Another intravenous urogram revealed ptosis of the left kidney.

Because the clinical picture simulated coarctation of the aorta, and because roentgenograms of the chest failed to confirm this belief, it was felt that aortography might reveal the exact nature of the lesion. Accordingly, this was done on March 23, 1945, puncture being made at the lower border of the twelfth thoracic vertebra. The aortogram (Fig. 5) revealed a sharply defined, complete transverse block at the left of the middle of the second lumbar vertebra, just below the origin of the renal arteries. No dye was visualized in the iliac arteries or lower portion of the abdominal aorta. A large anastomotic communication between the middle colic branch of the superior mesenteric artery and left colic branch of inferior mesenteric was well delineated, as in Case 1.

The day following aortography, the patient was discharged as unimproved.

Following the second discharge, the patient went back to his usual work as a waiter. Except for headaches and mild dyspnea on exertion he was able to work until January 28, 1946. At this time he experienced moderately severe substernal pain, radiating down the left arm, accompanied by dyspnea. These symptoms became severe on February 2, 1946, and on February 4, he was admitted to the hospital.

The patient was orthopneic, cyanotic, dehydrated, and poorly nourished. He was drowsy, but oriented and co-operative. The temperature was 100° degrees F.; pulse, 120; and respirations, 36. The blood pressure was 160/110 in the right arm but unobtainable in lower extremities. There were moist râles at both bases, but heart sounds were strong; no murmurs noted. There was moderate abdominal distention.

Blood count revealed a hemoglobin of 125 per cent, erythrocytes 5,400,000, leucocytes 14,000 with 90 per cent neutrophils, and 10 per cent lymphocytes. Urinalysis revealed occasional granular casts but was otherwise normal. The sedimentation rate was not increased. The blood nonprotein nitrogen was 75 milligrams and carbon dioxide combining power 20 volumes per cent. The electrocardiogram showed changes indicating an acute anterior coronary occlusion with involvement of a large posterior branch. The patient became progressively more dyspneic and died 33 hours later. During this final admission he voided only 200 cubic centimeters of urine.

Postmortem examination was performed by Dr. Peter A. Herbut. The salient gross pathologic findings were generalized arteriosclerosis, bilateral pleural adhesions, pulmonary congestion and edema, terminal pneumonia, cardiac hypertrophy, atherosclerotic thrombosis of the abdominal aorta both old and recent, and bilateral polar renal vessels. The heart, aorta, and kidneys were of the greatest interest and the findings in these are given in some detail:

The heart weighed 555 grams. The pericardial and endocardial surfaces were smooth and glistening. The myocardium was firm, hypertrophied, and reddish brown. There was no definite evidence of old or recent infarction. The valves were normal in number, size, shape, and position; coronary ostia patent, and vessels showed moderate atherosclerosis.

The thoracic aorta showed moderate atherosclerosis with several plaques. The abdominal aorta

showed a complete thrombotic occlusion extending from the renal vessels to the common iliac vessels (Fig. 6). The proximal 5 centimeters of the thrombus, extending equidistant above and below the upper renal vessels, was recent, dark red, friable, and only moderately adherent to the wall of the aorta in places. The portion extending from the lower renal vessels to the common iliacs, including the proximal 4 centimeters of the right common iliac, was dense, grayish white, fibrous, firmly adherent, and continuous with the wall of the aorta.

The kidneys weighed 130 grams each and measured approximately 12 by 7 by 5 centimeters. The capsules stripped with ease. The external and cut surfaces were deep reddish brown and the demarcations were sharp. There were 2 renal vessels to each kidney (Fig. 6). The upper renal vessels were 4 to 5 centimeters in length, 7 to 8 millimeters in diameter, and patent. The lower renal vessels were 4 to 5 centimeters in length, 2 to 3 millimeters in diameter, and occluded. The pelves and ureters were normal.

The salient histologic findings were pleural fibrosis, pulmonary congestion and edema, terminal pneumonia, myocardial fibrosis, atherosclerosis and thrombosis of the abdominal aorta, and benign nephrosclerosis.

Histologic sections of the lower portion of each kidney disclosed only slight ischemic atrophy. Sections through the upper portion showed severe congestion, severe arterial and arteriolar sclerosis, hyalinization of the glomeruli, proliferation of the glomerular epithelium, and occasional necrosis of the glomerular tufts. Sections of abdominal aorta at level of injection for aortography showed no changes that could be attributed to needle puncture.

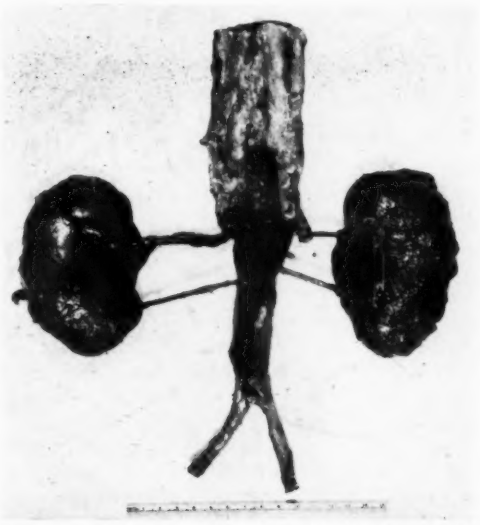

Fig. 6. Postmortem specimen of aorta and kidneys in Case 2, showing old thrombus below renal arteries and recent thrombus above renal arteries. Note bilateral polar renal arteries. Death occurred 10 months following aortography.

DISCUSSION

Visualization of the level and degree of arterial obstruction as well as the amount of collateral circulation following thrombosis and embolism is possible by means of arteriography. Although employed for this purpose in selected instances in the peripheral arteries (9), arteriography for diagnosis of aortic lesions has been practically neglected. According to a review of the literature on thrombosis and embolism of the abdominal aorta by Greenfield in 1943, there were 161 cases on record, and in none of these was aortography done to establish the diagnosis during life.

Blakemore (1) produced total occlusion of the aorta just distal to the renal arteries by wiring and electrothermic coagulation of a syphilitic aneurysm in this location. He then performed aortography by direct injection of 70 per cent diodrast solution into the lower thoracic aorta. The roentgenogram, which unfortunately was poor because of motion by the patient, nevertheless revealed radiopaque medium within both renal arteries, one very large collateral artery going down the right side posteriorly, opacification of wire within the aneurysm, and lack of visualization of the aortic bifurcation as evidence of complete obstruction. Farinas, (3, 4) by means of retrograde abdominal aortography has demonstrated partial and complete occlusion of the aortic cone. So far as we are aware, these represent the only previous reports of aortography in thrombotic occlusion.

It is interesting that, although the level of the block was identical in our 2 patients and both had hypertension, the symptomatology was different. In the first patient, the symptoms centered about the diminished supply of blood to the lower extremities, while in the second, the symptoms were principally related to the hypertension. In both symptoms were slow in onset, suggestive of a gradually narrowing process, but in the first the acute pain evidently represented completion of occlusion.

Collateral blood supply to the lower extremities in this condition is mainly by anastomosis

of the inferior with the superior epigastric artery, and by a paravertebral anastomosis of lumbar arteries (Fig. 3) with the deep circumflex iliac. The most important anastomosis among the visceral arteries is the middle colic with the left colic (Figs. 2 and 5), thus allowing the inferior mesenteric artery to receive blood from the superior mesenteric and preventing gangrene of the sigmoid colon.

The relatively long history in each case speaks for thrombosis rather than embolism. In spite of electrocardiographic evidence of coronary insufficiency in each case, there was no definite clinical evidence of infarction in the first patient, and no postmortem evidence of actual infarction in the second patient. It is probable that changes in the coronary arteries were merely part of the diffuse vascular disease. The first patient's age, peripheral vascular history, and absence of roentgenologic evidence of calcification in peripheral vessels or aorta, makes possible thromboangiitis obliterans as the cause.

The origin of the hypertension in these 2 cases is of interest. Goldblatt and Kahn studied experimentally the effect of constriction of the aorta at various levels. They found that constriction immediately above the level of the renal arteries produced persistent hypertensions above, on the basis of bilateral renal ischemia, and hypotension below. This corresponds clinically to the effects noted in coarctation of the aorta, namely, hypertension in the upper extremities and hypotension in the lower extremities. According to Rytand, experiments on albino rats show that the hypertension in coarctation of the aorta has the same pathogenesis as the hypertension in a dog with partially constricted renal arteries. On the other hand, constriction of the aorta immediately below the renal arteries produces no persistent hypertension, evidently because of the absence of renal ischemia. In Blakemore's case in which complete thrombosis was produced in an aneurysm immediately below the renal arteries, hypertension did not ensue (2).

On the basis of these experimental and clinical facts, the aortic block, *per se*, below the renal arteries as illustrated (Figs. 3 and 5) did not, apparently, account for the hypertension in our cases. Clinically, we felt the aortic block was a complication of the systemic vascular disease. However, at necropsy, the occlusion of the lower renal arteries (Fig. 6) resulted in bilateral renal ischemia as demonstrated by the histologic signs of ischemic atrophy. The renal ischemia could then be the basis of the severe hypertension seen clinically in the second patient. The patient's death was clinically that of heart failure hastened by propagation of the thrombus upward so the upper renal vessels were also partially occluded. In the first patient, although there is no definite proof, it is possible that the hypertension is also on the basis of renal ischemia, either due to occluded accessory renal vessels or the presence in the renal vessels of the same vascular disease which initiated the aortic thrombosis.

SUMMARY AND CONCLUSIONS

1. Two cases of complete aortic block immediately below the origin of the renal arteries, diagnosed during life by direct translumbar aortography, are reported in detail.

2. Thrombosis in this location, although a grave condition, is compatible with life. The propagation of the clot above the renal vessels leads to death, if the renal arteries are occluded.

3. Abdominal aortography should be more frequently employed as a diagnostic aid when a serious lesion is suspected and the usual studies fail to establish its true nature.

ADDENDUM.—The patient in Case 1 was readmitted to the hospital March 10, 1947. The aortogram made approximately 2 years after initial one revealed complete aortic block at same level and there was no change in collateral circulation.

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EXPERIMENTAL AORTIC VALVULOTOMY

A Preliminary Report

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THE possibility of a direct surgical approach to the problem of chronic valvular disease of the heart has been considered by surgeons for many years. Since the proposal of Brunton, in 1902, in which hope was expressed for the ultimate relief of mitral stenosis by surgical means, little of significance has been accomplished despite numerous clinical and experimental observations by several investigators. In an effort to develop a safe method of approaching the aortic valve, which conceivably might be applied to the surgical treatment of aortic stenosis in human subjects, aortic valvulotomy was performed in a series of dogs as described below.

It is not within the scope of this preliminary communication to review entirely the development of surgery of the heart valves. Suffice it to say that most observations heretofore recorded have concerned the clinical and experimental aspects of the production and relief of mitral stenosis. A complete review of the subject, including the earlier work of many physiologists, can be found in the extensive article of Cutler, Levine, and Beck (8). While very few studies have been reported on the production and relief of aortic stenosis, the latter investigators as well as Allen and Graham (2, 3) have mentioned, without elaboration, division of the aortic valves in dogs by means of a cardioscope. Tuffier (19) apparently made the only recorded attempt to relieve aortic stenosis in a human patient. His procedure consisted of digital invagination of the wall of the aorta into the ring of the aortic valve, thus dilating it, instead of incising the valve with a knife as he had intended to do at the outset of the operation.

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Recent progress in surgery of the heart and great vessels, notably the brilliant work of Blalock in pulmonic stenosis, Gross (10, 11) in coarctation of the aorta and Alexander and Byron in aortic aneurysm, has served as a stimulus in conducting the following experiments.

MATERIAL AND METHODS

Mongrel dogs were used. Anesthesia was obtained by the intravenous administration of sodium pentobarbital. The thorax was entered through an incision in the left fifth intercostal space, whereupon a previously inserted intratracheal catheter was attached to an artificial respirator delivering an interrupted flow of atmospheric air under positive pressure. Full exposure of the heart was obtained by self-retaining rib-spreading retractors. The pericardium was opened near the apex anterior to the phrenic nerve and incised vertically upward to its reflection from the ascending aorta. By blunt dissection, the proximal third of the ascending aorta was freed sufficiently to pass a ligature of medium sized silk around it. Traction on this ligature was used to deliver the first portion of the aorta into the wound when desired (Fig. 1). A small area of the presenting lateral surface of the ascending aorta next was denuded of its well defined fatty coat, the fat tissue being bluntly pushed aside without actually excising it. Either a stay suture of fine silk or catgut was then placed in the periaortic fat in the form of a pursestring or interrupted sutures in the fat were used (Fig. 1), the former proving the most satisfactory. In some animals an attempt was made to secure stay sutures in the wall of the aorta itself with discouraging results (Table II). Having placed the periaortic fat sutures, the denuded area of the aortic wall was punctured with a No. 11 Bard-Parker blade, producing a very small opening. Ensuing hemorrhage was controlled

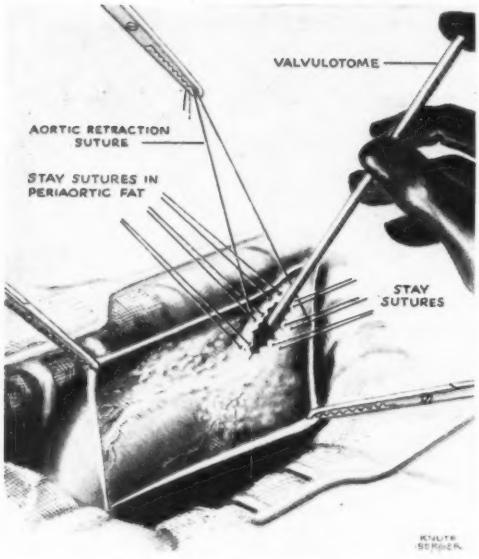

Fig. 1. Introduction of valvulotome into aorta after placing traction ligature around aorta and stay sutures in periaortic fat.

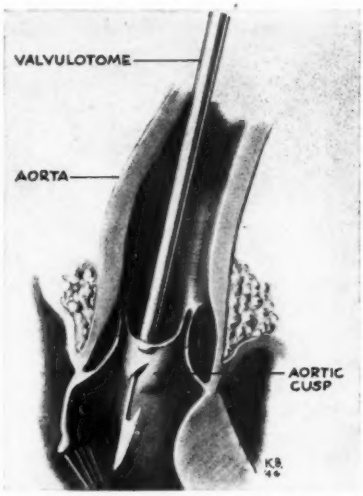

Fig. 2. Schematic representation of longitudinal section of aorta showing perforation of valve leaflet. Withdrawal upward of barbed blade divides free margin of cusp.

by digital pressure over the opening while the traction ligature was held taut thus bringing the exposed portion of the aorta into the wound and immobilizing it. A specially constructed valvulotome was then manipulated gently into the aortic opening and made to impinge upon the posterior wall of the aorta (Fig. 1). In contact with the latter, the instrument was passed proximally within the aorta, its sheath tamponading effectively the wound in the aortic wall until its further progress was arrested within a cusp of the aortic valve. The hooked blade next was forced out of the sheath, perforating the cusp in its dependent portion; then the valvulotome was withdrawn, thus dividing the free margin of the leaflet (Fig. 2). In this maneuver, the instrument was withdrawn as a whole, without pulling the blade back into its sheath. Upon withdrawal of the valvulotome, hemorrhage from the opening in the aorta immediately became a problem of considerable magnitude. Its control was attempted by two methods. At the beginning of the experimental studies, closure of the defect by interrupted fine silk sutures placed in the aortic wall was the method employed. This resulted in a high mortality due to failure of the sutures to hold with tearing of the wall, thus increasing the size of the wound to such an extent that uncontrollable hemorrhage ensued (Table II). The second procedure was found to be more effective. It consisted of digital tamponade of the bleeding point until the previously placed stay sutures or pursestring suture in the periaortic fat could be tied over an absorbable gelatin sponge, which was manipulated beneath the tamponading finger so as to lie immediately over the aortic opening (Fig. 3). Upon control of the hemorrhage, closure of the pericardium and of the thoracic incision was effected.

TABLE I.—MORTALITY

Number of animals	22
Survivals	14
Operative deaths	8
Mortality, per cent	36

TABLE II.—DEATHS DUE TO HEMORRHAGE: COMPARATIVE MORTALITY ACCORDING TO TECHNIQUES

	Number of animals	Deaths	Mortality
Aortic suture technique	7	5	71%
Gelatin sponge technique	15	3	20%
Totals	22	8	36%

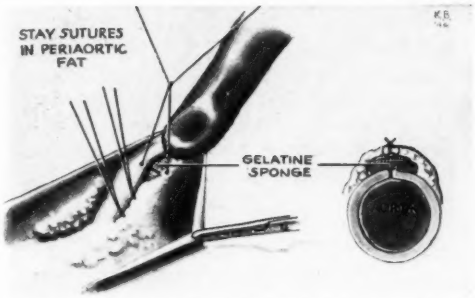

Fig. 3. Gelatin sponge secured over aortic wound by fat sutures.

Fig. 4. The conical sheath and barbed blade of the valvulotome.

Fig. 5. Beginning introduction of blade into sheath.

Fig. 6. The valvulotome completely assembled.

The valvulotome. The instrument used in producing the valvular defects consisted of two separate parts, the first being an exterior brass sheath of graduated, conical shape (Fig. 4), the smaller diameter being at the distal end, the larger at the proximal end. By this arrangement, tamponading of the aortic opening occurred as the distal end of the instrument was introduced into the aorta. The second part of the instrument consisted of a barbed blade attached to the end of a long brass handle (Fig. 4). The latter, upon being introduced into the sheath in the manner of a trochar into a cannula (Fig. 5), fitted snugly within the sheath so as to prevent the escape of blood around it. The interior of the sheath contained a circumferential ridge near its distal extremity which arrested further progress of the handle so as to permit only the blade to project from the distal end. Introduction of the sheath into the aorta was accomplished in each instance with the blade pulled up within the sheath so as not to damage the interior of the aorta during the downward progress of the instrument toward the valve leaflet. The blade was thrust out only after the sheath had become engaged within the cusp (Fig. 2).

RESULTS

Twenty-two animals were subjected to operation. There were 14 survivals and 8 deaths, a mortality of 36 per cent (Table I). All deaths occurred either during the operation or immediately thereafter and were due in each instance to severe blood loss from the aortic wound. No attempt was made to replace blood by transfusion, a fact which undoubtedly influenced the outcome in some cases. Table II summarizes the comparative mortality according to techniques employed to control hemorrhage from the aortic opening. In the first 7 animals operated upon, stay sutures of fine silk were placed directly in the wall of the aorta instead of in the periaortic fat. Five of these animals died of hemorrhage because the sutures failed to hold, cutting through the aortic wall and producing large rents which grew larger as further efforts at direct closure by suturing were made. Fifteen animals were operated upon with only 3 deaths (Table II), using the combination of periaortic fat suture and gelatin sponge tamponade of the bleeding point. A pursestring suture in the fat was found to be superior to interrupted stay sutures. The 3 deaths in the group treated by the fat suture-gelatin sponge technique resulted from hemorrhage incident to one or both of two factors: slipping of the sponge from its proper location during closure of the overlying fat and accidental enlargement to an unmanageable extent of the aortic opening during introduction of the valvulotome.

The 14 surviving animals were sacrificed at intervals varying from 24 hours to 7 days after

TABLE III.—VALVULAR LESIONS PRODUCED IN SURVIVING ANIMALS

Surviving animals	14
Perforation of cusp	8
Division of cusp	4
Absence of lesion	2
Successful results, per cent	86
Failures, per cent	14

operation. Valvular lesions were found in 12 animals (86%). In 2 animals, no evidence of a valvular defect was noted (Table III). In the latter it is likely that the valvulotome failed to become engaged in a leaflet, passing instead into the ventricular chamber during systole. Perforation or laceration of a cusp occurred in 8 animals, while in only 4 animals was complete division of the free margin of the leaflet produced (Table III).

DISCUSSION

Of the technical aspects of the procedure described, two features deserve special comment: first, the effect of simple division of an aortic valve leaflet upon the ultimate course of aortic stenosis in the human and, second, the gelatin sponge tamponade method of controlling hemorrhage from a wound of the aorta. Regarding the former, only hypothetical considerations are permissible from this preliminary report. As noted by Cutler and Beck (9), the presence of marked thickening, rigidity and calcification in the aortic valve in cases of stenosis would indicate that valvulectomy, rather than valvulotomy, may be necessary to alter favorably the circulation in these cases. Furthermore, an estimate of the effect of either procedure is difficult in the absence of a satisfactory method of producing aortic stenosis in the experimental animal. Further experimentation in this field is indicated.

Concerning the gelatin sponge method of tamponading hemorrhage from the aorta, one might regard the technique employed as being relatively insecure. While it would appear that direct suture of the aortic wound is preferable, a lower mortality resulted in those animals treated by the gelatin sponge method. These findings are in keeping with the work of Jenkins (14, 15) and his associates whereby the successful use of absorbable gelatin sponge was demonstrated in controlling hemorrhage from wounds of the heart, aorta, and vena cava in experimental animals.

SUMMARY

With a view toward its possible application to the treatment of aortic stenosis in human subjects, a technique of aortic valvulotomy in dogs is described.

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ARTERIOVENOUS FISTULA: EXPERIMENTAL STUDY OF INFLUENCE OF SYMPATHETIC NERVOUS SYSTEM ON DEVELOPMENT OF COLLATERAL CIRCULATION

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UP to the time of John Hunter, the ligation of a major vessel had been avoided because it was a fearful procedure in the treatment of aneurysm owing to the high incidence of infection, gangrene, and secondary hemorrhage. Not until the early part of the nineteenth century was the concept accepted that collateral vessels were able to take over the function of a major artery in supplying adequate nutrition to the tissues. The high incidence of recurrence of symptoms, as well as the development of severe trophic disturbances and gangrene, after simple ligation of the artery proximal to the arterial and arteriovenous aneurysm (Anel ligation), led Makins in 1914 to suggest the simultaneous ligation of the companion vein. Further experimental and clinical studies of arteriovenous fistula by Holman (19–21, 23, 24), Reid (40, 43), Pemberton and others (36, 37) have established quadruple ligation and excision of the vascular lesion as an adequate means of treatment. Since a relatively small proportion of cases have been suitable for treatment by the Matas restorative endoaneurysmorrhaphy or the Blakemore-Lord type of vein graft, we must be ultimately concerned with the degree of collateral circulation that results from an abnormal communication between a major artery and vein. Reid (42) in 1925 stated that the arteriovenous fistula is the most powerful stimulus to the development of collateral circulation known, and consequently urged that sufficient passage of time should be allowed to permit the development of adequate collateral circulation. The factor of time has been similarly emphasized by Matas, Holman, and by Pemberton and Black (36), Elkin and many others.

It should be pointed out, however, that an arteriovenous communication acts entirely differently from other types of vascular lesions, which usually cause more or less obstruction with a resulting rise in resistance to the flow of blood through the affected vessels. In an arteriovenous fistula, on the other hand, the blood in the arterial system, on arriving at the fistula, enters a region of markedly reduced resistance and flows directly into the vein, where its distal movement is obstructed by valves, by the decreasing caliber of the vessels and by elevated venous pressure. The blood consequently returns immediately to the right side of the heart, thus by-passing the distal arteriolar and capillary beds. The shunting of the arterial blood, when sufficiently great, obviously deprives the distal tissues of the involved part of adequate nutrition and stimulates compensatory responses. To quote Holman (22), "All avenues of approach to the fistula open up to appease, as it were, the thirst of the fistula."

As stated in the preceding paragraph, one important factor in disrupting normal vascular physiologic processes in a part distal to an arteriovenous fistula is the rise of venous pressure. It is obvious that the arterial blood, under a tension of more than 100 millimeters of mercury on entering the venous system via the fistula will cause an elevation of the venous pressure which by contrast normally may be measured as a few centimeters of water. The mechanical obstructions to distal venous flow of this arterial blood, mentioned previously, are effective in diverting the greater part of the flow proximally toward the heart. This increase of volume flow and pressure results in a

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compensatory dilatation which is demonstrable in the centripetal venous channels as well as the right side of the heart. Distally in the extremity this elevated venous pressure also hinders circulation from collateral vessels that otherwise would be much more effective.

The presence of a region of markedly elevated venous pressure at the fistula serves to act as a block to the venous outflow of the distal parts by virtue of the pressure differential as well as the effect of keeping the distal valves in the veins shut. Since the normal direction of the arterial systolic thrust is centrifugal, there is maintained a constant piston-like force on the distal venous tree, so that eventually as a result of the distention of the vessels and the direct pressure on the cusps, the valves may become incompetent. The magnitude of this effect depends primarily on the duration, size, and location of the fistula. Secondary to this interference with normal venous drainage is an increase of the intercellular fluid and lymph. The scarring about a traumatic fistula may block some of the major lymphatic channels and thus contribute to the formation of edema.

Hence, in the presence of a fistula, the distal parts are frequently deprived more effectively of a normal circulation than following actual ligation of the major artery or arteriectomy. That the so-called collateral circulation is unable to provide an adequate blood supply to the tissues is evidenced by the frequent occurrence of trophic alterations in the distal parts. Trophic changes are seen as well in persons who have congenital arteriovenous fistulas even when the maximal time for development of collateral circulation has elapsed. While gangrene is relatively rare following closure of an arteriovenous fistula in the lower extremity, there is a high incidence of vascular insufficiency, particularly in the aged, which is manifested by chronic edema, intermittent claudication, ease of fatigue, sensation of heaviness and paresthesias. This was noted by Bigger, who saw in his postoperative cases "definite evidence that circulation is inadequate for sustained muscular activity. This is an important matter, and one which has not received the attention which is its due." Other authors have seen fit to question the value of this type of vascular response. La Roque in 1921 expressed the opinion that there was "much reason for believing that the development of circulation is antagonized by arteriovenous fistula." Elkin (8) in 1943 similarly pointed out the possible inadequacy of this collateral circulation when he said that this great collateral circulation was for the most part useless since the blood returns to the heart without nourishing the distal parts. Recently, Freeman has called further attention to the vascular deficiency which may follow the surgical repair of arteriovenous fistulas. In the March 8, 1947, issue of the *Journal of the American Medical Association*, Heringman, Rives and Davis reviewed the results of the various operative procedures employed in a series of 53 cases of arteriovenous fistula. Local vascular insufficiency did not develop in any of the 8 patients treated by a restorative procedure, whereas a third or more of those patients having an obliterative procedure suffered subsequently from the symptoms of vascular deficiency.

The acceptance by so many surgeons of the concept that great collateral circulation develops with time generally has resulted in a delay of 3 to 6 months in the treatment of arteriovenous fistulas. Consequently we were stimulated to attempt to determine the actual effective arterial collateral circulation present in a limb which had had a fistula functioning for periods of time up to one year. Furthermore, because of the claim of some investigators that attempts to improve collateral circulation (after time enough has elapsed for it to have developed) are foolhardy if not actually contraindicated, an investigation was made of the cutaneous temperature in the limb distal to a long-standing arteriovenous fistula, both before and after lumbar sympathetic ganglionectomy.

I. DEMONSTRATION OF COLLATERAL CIRCULATION IN A LIMB IN WHICH THERE IS A CHRONIC ARTERIOVENOUS FISTULA

Method. In 19 adult dogs under ether anesthesia, lateral arteriovenous fistulas were made, in the femoral vessels, 1 to 2 centimeters below the profundus branch of the artery by the suture method (7). The communication between the artery and the vein ranged from 1.5

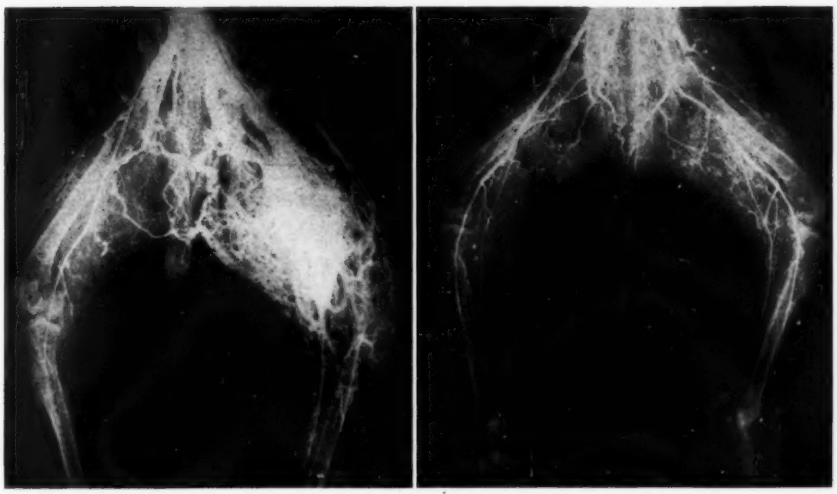

Fig. 1. a, left, Arteriovenous circulation of the left hind limb of an animal in which an arteriovenous fistula had been present in the femoral vessels for more than 6 months. b, Isolated arterial circulation after excision of a fistula of 7 months' duration.

to 3.0 centimeters in length. In no case was there ever an occlusion by thrombosis or healing. The effectiveness of the fistula could be shown by subsequent alterations of cutaneous temperature, progressive increase of total blood volume (modification of the technique of Gibson and Evelyn using the diazo dye, T1824), and enlargement of the heart (measurement of cardiac silhouette by planimeter) over an ensuing period of 8 to 10 months. At the conclusion of the period of observation, the animals were killed. The first 12 animals comprise series A. This series was divided into 3 groups and the anatomy of the vascular tree of the limb was studied in the manner now to be described.

Series A. Group I. Method. Immediately after death, the abdomens of 4 animals were opened in the midline and the great vessels were carefully exposed. Both the aorta and the vena cava were cannulated midway between the renal vessels and the trifurcation of the aorta. The limb was perfused at once with warm Ringer's solution which was injected into the aortic cannula with a Dale-Schuster pump. The perfusion was continued until the outflow from the vena cava was relatively clear. To insure the complete flushing of the vascular tree, the fistula was occluded by digital pressure until the final period of the irrigation. An injection mass (barium sulfate, 300 gm.; saturated solution of acacia, 100 c.c.; and distilled water, 200 c.c.) was then used to fill the vascular bed. This material was injected into the aortic cannula with a 50 cubic centimeter syringe. The fistula was kept occluded until back pressure was felt on the plunger of the syringe. Digital pressure over the fistula was then released and the entire functioning circulatory bed was filled with the barium suspension. When this material flowed from the vena caval cannula, this outlet was clamped and 5 cubic centimeters more injected. Then, with the aortic cannula also clamped, roentgenograms were made of the lower vascular tree.

Results.—There was well demonstrated a heavy network of dilated tortuous vessels, composed in part of arteries but mostly of veins, in the left thigh, where the fistula had been produced (Fig. 1*a*). The lower leg and foot did not have any such distended vessels. The artery and vein proximal to the fistula were frequently dilated to a moderate extent, and this process involved the vena cava as well. This was the result of a prolonged in-

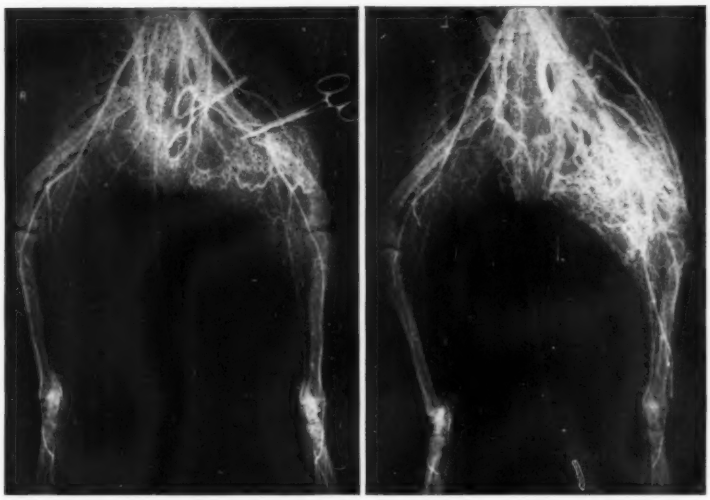

Fig. 2. a, left, Isolated arterial collateral circulation after occlusion of the abnormal communication with Carrel clamps. b, The same animal after removal of the clamps and completion of the injection with the fistula patent. This indicates that the predominant vascular response has been venous.

crease of venous pressure and blood flow. This "Medusa's head" in the region of the fistula is what many authors have referred to when they described the collateral circulation of an arteriovenous fistula. This is also an example of what one sees in a clinical angiogram of this type of lesion, for the patent communication allows the contrast medium to fill the entire network of vessels and permits identification of the fistula. It must be realized that a clear picture of the arterial circulation is necessary to evaluate collateral circulation. Any obliterative surgical procedure will close the communication between the artery and the vein, and consequently exclude the dilated venous vessels from the collateral vascular supply. To demonstrate the isolated arterial bed, the following procedure was used.

Group II. Method.—In 4 animals the perfusion with Ringer's solution was carried out as described. The fistula was then exposed by cautious dissection without sacrifice of any major collateral vessel. The proximal artery and vein were identified and ligated adjacent to the site of the fistula. The distal vessels were similarly ligated and the fistula was excised. In all instances the arteriovenous communication had been patent up to the time of closure. Injection was then carried out to demonstrate the arterial system alone.

Results.—In this series, a representation of the venous response to the presence of a chronic arteriovenous fistula was eliminated completely by excision of the fistula. The injected vessels represented only the arterial channels in the limb. These in turn were the true collateral circulation or that part of the circulation which would function after surgical closure of the fistula (Fig. 1*b*). The marked contrast in the appearance of the vessels before and after closure of the arteriovenous fistula cannot be overemphasized. However, it must be admitted that there was a marked difference in the appearance of the injected vascular beds of successive animals. In some of the animals, except for the region from which the fistula had been excised, the arterial tree was approximately the same in the control limb as in that with the fistula. On the other hand, a number of animals that had fistulas of the same size and duration had a definite augmentation of arterial circulation just distal to the fistula. With such variation possible, it was therefore necessary to compare in the same animal the

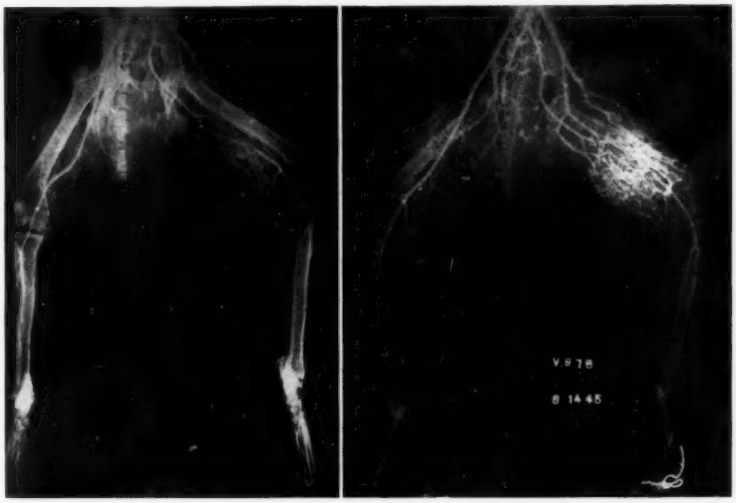

Fig. 3. a, left, Two weeks after bilateral lumbar sympathectomy, showing the isolated arterial collateral circulation (made immediately after excision of a fistula of 7½ months' duration). *b*, Two weeks after unilateral lumbar sympathectomy performed on the side of the fistula (left). In this case the picture was taken immediately after excision of a fistula of 7½ months' duration.

isolated arterial tree with the complete arteriovenous bed.

Group III. Method.—The legs of the 4 remaining animals of series A were perfused in the usual manner, and the fistula was dissected free. Carrel clamps were placed on the proximal and distal vessels to occlude the arteriovenous communication effectively. Injection was then carried out and roentgenograms of the isolated arterial circulation were made. Later, the clamps were released and the injection of the barium mass was completed as in group I. Roentgenograms were again taken.

Results.—This set of experiments showed clearly the paucity of arterial collateral circulation compared with the total vascular bed in the region of the fistula (Fig. 2*a* and *b*) in the same animal. A differential study of this kind in a group of animals having comparable fistulas of varying duration makes possible an understanding of the rate of development of the vascular changes. It is evident that the arterial response appears very rapidly, reaching its maximal development early, while the augmentation of the venous system is gradual, occurring during a period of many weeks.

Series B. Method.—The remaining 7 animals were also used in a study of the effect of lumbar sympathetic ganglionectomy on blood flow and cutaneous temperature. In 4 animals, bilateral lumbar ganglionectomy was performed, and in 3 the ganglionectomy was restricted to the side of the fistula. In all the animals, the arteriovenous communication had been active for about 7 months before sympathectomy. In this series the fistula was excised 2 weeks after sympathectomy (a) to demonstrate further the isolated arterial system as an entity and (b) to show any effect on this system that sympathectomy might have had. Immediately after the quadruple ligation and excision of the fistula, the injection of the isolated arterial tree was carried out as described for group II.

Results.—Roentgenograms were made of the lower arterial vascular bed of the sympathectomized animals after perfusion and injection. In the group on which bilateral lumbar ganglionectomy had been performed 2 weeks previous to the excision of the fistula, there was a minor degree of vasodilatation and tortuosity of the small arteries just distal to

the region of the aneurysm (Fig. 3*a*). This was seen also in the series without sympathectomy and represents the degree of arterial response primarily as a result of time. As the denervation had been bilateral, there was no significant gross difference in the general vascular bed of both limbs beyond that resulting from the aneurysm alone. The differences of cutaneous temperature of the limbs found are reported farther on in this paper. They were accounted for on the basis of differences in the circulation supplying the limbs.

In the animals which had sympathectomy only on the side of the fistula, there was a slight increase in diameter of the vessels on the denervated side over that of the control side. In all these animals, the greatest apparent increase was in the region just distal to the excised fistula (fig. 3*b*), since here there were superimposed the outlines of those many small arteries which had dilated as a result of the aneurysm. However, further evidence that the vasodilatation following sympathectomy affected the entire vascular segment will be presented in the section of this report dealing with cutaneous temperature.

Comment. A comparison of roentgenograms taken on animals having arteriovenous fistulas of shorter duration than the fistulas of the dogs already considered indicates that the arterial response is rapid, requiring only a few days to be significant. This is in agreement with studies on the development of collateral flow by other investigators which have shown most of the channels involved in collateral circulation to be present at the time of an obstruction of a major vessel. The venous component of the circulation resulting from an arteriovenous fistula, on the other hand, develops more slowly and relentlessly over a period of weeks or months, and is without beneficial effect on the limb. Concurrent with the local dilatation of the venous bed there are increases of circulating blood volume and cardiac size. Experimentally, we have found microscopic evidence that there are pulmonary, renal, cardiac and hepatic changes which may or may not be reversible.

On inspection of the arterial collateral circulation developed during a period of more than six months, it is important to note that the localized region of increased vascularization is actually *distal* to the arteriovenous fistula. It would appear therefore that the small arteries, visualized by injection methods, had been subjected to an excessive function, but in a manner different from the usual collateral channels which develop in response to an obstructive lesion. The tremendous return flow of blood from the fistula toward the heart indicates that the dilated channels in the arterial system have been draining blood into the site of the fistula with its low pressure by diversion of much of the blood which flows normally to the pelvic structures and limb via anastomotic channels of the deep circumflex iliac, internal and external iliac, pudendal, gluteal and lateral sacral vessels among others. One may consider as well the possibility that when reversed venous flow occurs, some of this blood finds itself back in arterial channels, and by retrograde flow again enters the site of the fistula. Consequently, with the fistula patent, these channels do not serve to by-pass the lesion and act as supplementary vessels as in obstructive vascular lesions. In the latter, by contrast, the accessory vessels have their greatest function and are the most numerous in the actual region of obstruction. They arise from the immediately adjacent derivatives of the affected vessels, particularly from the proximal branches. Consequently, it is difficult to escape the belief that the arterial collateral circulation in the presence of an arteriovenous fistula may contribute much less to the subsequent viability of the limb after obliterative operation than is ordinarily believed. The rise of cutaneous temperature of the toes observed (5,41) after closure of a more proximal fistula is but a qualitative and not a quantitative index of the increase of distal blood flow. Consequently, this rise of cutaneous temperature gives no indication of the actual amount of collateral circulation. That this increase of blood flow may be inadequate is attested by the reports of gangrene and circulatory deficiency following the repair of a fistula.

One would expect the beneficial effects of lumbar sympathetic block on collateral circulation to involve the entire limb, in contrast to the response of the vessels to time alone, in which latter case the dilatation would very

probably be localized in the region of the fistula. To test this concept, as well as to determine the degree of influence that the sympathetic nervous system has on a limb subjected to the physiologic changes attending an arteriovenous fistula of long standing, we made studies on cutaneous temperatures as an indirect index of digital arterial blood flow.

I. STUDIES OF CUTANEOUS TEMPERATURES OF ANIMALS HAVING CHRONIC ARTERIOVENOUS FISTULAS: BEFORE AND AFTER LUMBAR SYMPATHECTOMY

Experimental studies (6, 11, 45, 46) have proved that under certain conditions the cutaneous temperature of the paw of an animal may be taken as an indication of the distal arterial blood flow. Consequently, alterations of significant magnitude following sympathetic denervation should similarly serve as an acceptable indirect index of blood flow.

Methods. Two recording devices were employed in the measurement of cutaneous temperatures: (1) the Tycos dermatherm, a galvanometric apparatus with thermocouples adaptable to flat skin surfaces and (2) a mercury-bulb chemical thermometer, used for measuring the temperature between the toes of the animal. Readings were taken in triplicate and careful control of the environmental variables was exercised, as advocated by Sheard (45) and Roth. A constant air temperature of 26 degrees C. was maintained and the humidity was kept at 40 per cent. Linear air movement was limited to 15 to 30 feet (4.6 to 9 meters) per minute. The skin surface was always dry, clean and smooth shaven. The animals were kept comfortably recumbent for one hour to allow adjustment of the vasomotor system to a constant temperature. They were fasted 18 hours to exclude metabolic effects and the readings were taken at the same hour each morning to avoid diurnal variation.

These studies were performed on the same group of 19 animals used for the arteriographic studies already described. During the 8 to 10 month period of observation the increase of circulating blood volume (average increase of 31 per cent) and heart size (average increase of 32.5 per cent) was noted. Together with the signs of arteriovenous fistula—vibratory continuous thrill, machinery murmur, distended pulsating venous channels, bradycardiac reflex, and so forth—there was adequate evidence that the fistula was patent during the entire time.

TABLE I.— AVERAGE TEMPERATURE GRADIENT OF THE HIND LIMB OF AN ANIMAL HAVING A CHRONIC LEFT FEMORAL ARTERIOVENOUS FISTULA

Site of measurement	Right	Left
a. Before bilateral lumbar sympathetic ganglionectomy		
Poupart's ligament	37.0° C.	37.5° C
Thigh:		
Upper third	37.0	38.5
Middle third	36.0	38.0
Lower third	35.0	37.5
Lower leg	33.0	34.5
Ankle	32.5	32.0
Foot	32.0	31.0
Interdigital web	31.5	30–30.5
b. After bilateral lumbar sympathetic ganglionectomy		
Poupart's ligament	37.5	38.0
Thigh:		
Upper third	37.5	39.0
Middle third	37.0	38.5
Lower third	36.5	38.0
Lower leg	36.0	36.5
Ankle	35.5	36.0
Foot	36.5	36.0
Interdigital web	37.0	35.5

Results. The average normal temperature gradient as determined by cutaneous thermocouple readings on the medial aspect of the hind leg of a normal animal, from Poupart's ligament to the toes, was recorded. These values are those obtained on the control or right hind limb of the animals having left femoral arteriovenous fistulas (Table I, a). From a temperature of 37.0 degrees C. obtained at the groin of the normal limb, there was a gradual decrease distally to 31.5 degrees C. as measured in the interdigital web of the foot. On the leg with the fistula the temperatures ranged from 37.5 degrees C. at the groin to 30.0 to 30.5 degrees C. at the toes. In this limb, however, the thigh was warmer than proximally in the groin because of the presence of the aneurysm (38.5° C.). This effect by virtue of increased vascularity in the region of the aneurysm has been utilized clinically to localize a fistula. The great distention of superficial vessels made this entire thigh warmer than on the control side, but there was a rather sharp decrease of temperature of the ankle and foot to a value below that of the normal side.

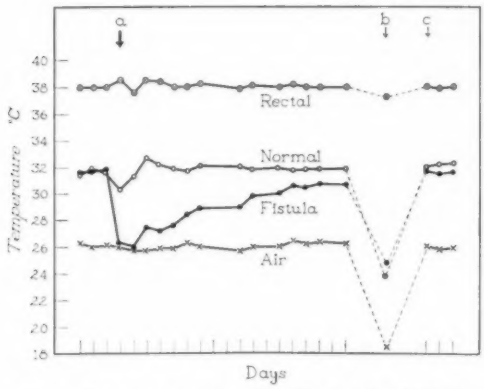

Fig. 4. Cutaneous temperature of the toes, in addition to rectal and air temperatures: *a*, the operative production of a left arteriovenous fistula; *b*, cool room experiment; *c*, quadruple ligation and excision of the fistula.

Having demonstrated by arteriograms that these dilated channels did not extend to the foot, we could depend with considerable confidence on temperature changes of the toes as being a reliable index of arterial flow.

In order to follow these changes closely, cutaneous temperatures of the toes were measured daily following the establishment of an arteriovenous communication in the left femoral vessels. Concurrent recordings were made of the rectal and air temperatures in order to note excessive variations of temperature in the body or in the environment. The control values noted prior to the vascular operation were rather constant (Fig. 4). Immediately after the production of an arteriovenous fistula, there was a sharp drop of toe temperatures of the limb on which operation had been performed almost to room temperature (Fig. 4*a*). This was due to (1) vasospasm resulting from manipulation and (2) the distal ischemia due to the blood flow into the low pressure region at the fistula rather than to the tissues beyond. During the next day there was a sharp rise of the temperature of the leg with the fistula of about 2 degrees C., probably representing a decrease of vasospasm that had resulted from the operation. The normal leg and rectal temperatures rose slightly as evidence of a general reaction to the operation. This lasted but 1 to 3 days, and thereafter these temperatures followed the normal levels (toe = 31.5° C. average; rectal = 38.0° C. average). During subsequent days the toe temperature of the limb with the fistula increased but became relatively constant about 1.0 degree to 2.0 degrees C. below the control temperature of the right limb, in 7 to 12 days.

In the subsequent period the response of the limbs to an abnormally cool environment was studied (Fig. 4*b*). On several occasions each animal was exposed to air temperature of 18 degrees C. for 30 minutes, and 15 minutes after removal of the animal to a room at about 26 degrees C., the temperature of the toes was recorded. It is significant that the normal side responded most efficiently to alterations of external environment. This greater vasoconstrictive ability of the normal limb made the leg with the fistula seem relatively warmer.

In some of the animals, quadruple ligation and excision of the fistula was performed after six months. A rise of toe temperature of the fistulous leg was noted on excision of the communication (Fig. 4*c*). This was probably due to redistribution of arterial blood with a more normal blood flow through the distal capillary beds.

Effects of sympathectomy. After a period of 7 months had been allowed for definite physiologic changes to have taken place, so far as the general and local cardiovascular systems were concerned, 7 dogs were selected from the group and repeated preoperative temperature readings were taken (Fig. 5 up to *a*). Prior to a sympathectomy, the animals were given ether anesthesia in an effort to simulate the effects of the operation, since Herrick and associates and Baldes and associates had showed that the 2 procedures caused an identical increase in blood flow in the femoral artery of the dog. We soon discovered that under light ether anesthesia, there was a lag in vasodilatation in the limb with the fistula, the rise in temperature being only about 2.5 degrees C. instead of the 5.5 degrees C. average of the normal side (Fig. 5*a*). This lessened response was shown to be a "lag" rather than organic inability to respond, since under deep ether anesthesia (or lumbar sympathetic ganglionectomy) the temperature of the leg with the fistula continued to rise to a total average of 4.5 to 5.0 degrees C. higher than before anes-

thesia or operation (Fig. 5*a'*). This functional change in the response to stimuli, which normally call forth a high degree of vasomotor activity, had been similarly seen previously in the cool room experiment in which the abnormal limb did not constrict as well as the normal limb. This abnormal response may be explained by (1) altered distribution of blood volume in the limb, (2) the abnormal rôle of venous channels in carrying arterial blood, and (3) disturbance of the functional and structural characteristics of the vessels as a result of long-standing effects of the fistula.

A number of preliminary trials with ether anesthesia demonstrated this delayed response of the abnormal leg to be a constant finding. Despite the evidence of good "collateral" circulation, we performed our operative removal of the lumbar sympathetic ganglia (L2 to and including L5) with the intervening chain by a transabdominal route. In 4 animals, the extirpation was bilateral in one stage so that there might be a control side with which to compare the physiologic response to sympathectomy. In the remaining 3, the procedure was carried out only on the side on which there was a fistula. This would more clearly reveal the results to be expected from clinical application of sympathectomy to a limb having an arteriovenous fistula.

Cutaneous temperatures of the toes and entire limb were obtained after the sympathetic denervation and these observations were recorded daily thereafter for more than two weeks. Then, after a cool room test, the fistulas of 2 animals from both groups were excised after quadruple ligation.

Bilateral sympathectomy.—Before sympathectomy, the previously normal right leg showed a marked gradient of from 37.0 degrees to 31.5 degrees C., whereas after sympathectomy, the skin surface of the entire limb was close to 37.0 degrees C., being lowest (35.5° C.) at the ankle (Table 1*b*). This demonstrated a maximal response of the cutaneous vessels to vasomotor denervation. The left limb, which had had an arteriovenous fistula in the thigh for 7 months, responded in much the same manner except for quantitative differences. As before sympathectomy, the thigh and leg were warmer than those of the

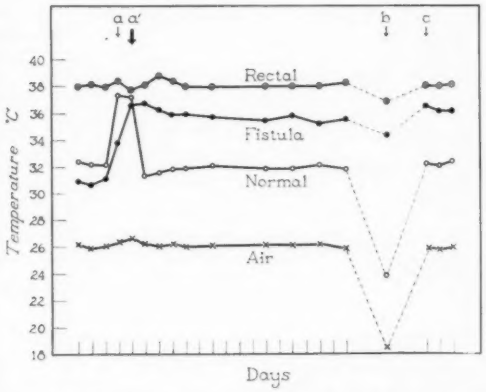

Fig. 5. Cutaneous temperature of the toes of the normal foot and of the leg with the fistula, 7 months after its production, in addition to rectal and air temperatures: *a*, response to light ether anesthesia; *a'*, deep ether anesthesia and concurrent left lumbar ganglionectomy; *b*, cool room experiment; *c*, quadruple ligation and excision of the fistula.

control limb, but the foot and toes were 0.5 to 1.5 degrees C. cooler than those of the control sympathectomized side. This relationship of toe temperatures therefore continued to be constant, even after sympathectomy, indicating the rôle the fistula plays in preventing a normal distal blood flow, regardless of environment or vasomotor activity.

Following the bilateral sympathectomy, the same elevation of cutaneous temperatures of the toes was recorded as was obtained when the animals were under deep ether anesthesia preliminary to both unilateral and bilateral sympathectomy (Fig. 5*a'*). During the succeeding 2 weeks, however, the temperature of both limbs decreased gradually about 1.0 to 1.5 degrees C as measured between the toes.

When these animals were given the cool room test, that is, exposure to an air temperature of 18 degrees C. for 30 minutes, neither limb showed significant evidence of vasoconstrictive ability. In 2 of the animals that had bilateral sympathectomy of 2 weeks' duration, the fistula was isolated and removed by quadruple ligation and excision. It was immediately noted that the removal of this communication was attended by a slight but significant rise in toe temperature, to almost the equal that of the control side. This is explained by a redistribution of arterial blood through the distal arteri-

olar and capillary beds as a result of removing the arteriovenous communication.

Unilateral sympathectomy.—As in the preceding experiment, concurrent readings were made of both hind limbs, rectal and air temperatures (Fig. 5). These results represent the type of response one may expect in the clinical application of lumbar sympathectomy to patients having arteriovenous fistula of the leg.

The response to ether anesthesia in this series of animals was again identical with that previously described for the animals in other series. Under light anesthesia, a "lag" in the temperature rise was noted in the limb with the fistula compared to the immediate complete response of the control normal limb (Fig. 5*a*). With deep ether anesthesia, the temperature continued to rise to a level about 1.0 degree C. below that of the normal side (Fig. 5*a'*). At this point left lumbar ganglionectomy was performed.

After recovery from ether anesthesia, the temperature of the control limb fell to the preoperative level or slightly lower, indicating in some instances a contralateral vasoconstriction. This latter phenomenon was only transient, however. On the sympathectomized side the elevated cutaneous temperature persisted at a level of about 37 degrees C. During the subsequent 2 weeks this significant rise of toe temperature was maintained with only a slight decline to about 36.0 degrees C., or an elevation of 3.0 to 4.5 degrees C. over that of the normal control side (Fig. 5*a'* to *b*). This fact demonstrated conclusively that the vessels distal to the fistula were indeed capable of further vasodilatation even after a period of 7 months in which collateral circulation had developed.

As in the other groups, these animals were given the cool room test; there was only a slight fall of about 1.0 degree C. in the temperature of the sympathectomized limb as compared with a decrease of temperature of more than 8 degrees C. in the normal limb (Fig. 5*b*). This is clear evidence that an anatomic interruption of the vasomotor nerves had been accomplished by the sympathetic ganglionectomy.

Two animals were selected from this group. Two weeks after the unilateral sympathectomy, the fistula was excised by quadruple ligation and excision. Once again, a slight but significant rise of toe temperature was observed, indicating increased distal arterial flow after obliteration of the fistula (Fig. 5*c*).

Comment. It is evident that our experiments have indicated that the blood flow in a limb may be significantly increased in the presence of a chronic arteriovenous fistula of a major peripheral artery following sympathetic denervation. The adequate treatment of arteriovenous fistula depends primarily on the condition of the collateral blood supply when an obliterative procedure is the method of choice. Naturally, the secondary factors of general condition of the patient, his cardiac status and presence of infection or nerve involvement are important but in the presence of insufficient blood supply, little choice remains to the surgeon beyond temporary vein ligation, amputation, or in certain cases, restorative endoaneurysmorrhaphy. In any operative procedure in which the arteries are involved, one runs the ever present danger of disastrous vasospasm as a result of the surgical manipulation. The present-day safeguards against thrombosis, such as precise aseptic technique, improved antibiotic agents and the anticoagulant drugs, heparin and dicoumarol, have made direct repair or ligation of major peripheral arteries a less formidable procedure than in the past century, or even during World War I.

There is considerable evidence, both direct and indirect, that the majority of channels composing a collateral system are in existence, even though relatively inactive in the normally functioning part. In the dog, many investigators have demonstrated by arteriography the ready appearance of supplementary arterial channels when obstruction had occurred in various regions; Vvedenski, in the hind limb; Kolesnikow, in the fore limb; Andreyev, in the head.

The demonstration of the great differences in the arterial and arteriovenous bed in the limbs of our animals that had fistulas raises the question whether a surgeon is justified in waiting several months for collateral circulation to develop before closure of a fistula in a patient. Mason (30) and Mason, Graham and

Bush (32) have reported cardiac failure in a period of only a few days or weeks after the development of a traumatic fistula. Fick found some of the vascular alterations irreversible and argued for early operation on patients who have arteriovenous fistula. Harbison has similarly urged early operation after employing sympathectomy to increase the collateral circulation so that frequently associated nerve injuries can be repaired easily. Elkin (9, 10) reported early operation to have been performed frequently on soldiers without even sympathetic block being necessary. However, the important effect that sympathectomy exercises on the full development of collateral systems has been emphasized by Mulvihill and Harvey. They concluded that "at least the interruption of efferent vasomotor impulses by ganglionectomy initiates the establishment of the collateral circulation, and to all appearances in the same manner as it occurs after a time of itself."

The first clinical application of this fundamental principle was reported by Gage (14) in 1933 in the treatment of a mycotic aneurysm of the iliac artery. By paravertebral sympathetic block, the circulation in the limb was increased sufficiently to allow ligation of this large vessel with impunity. Subsequently in 1939 (15) he stated that he "had similar and satisfactory results with arterial and arteriovenous aneurysms."

Bird in 1935 was perhaps the first to report the preoperative use of sympathectomy, preparatory to the repair of a major peripheral aneurysm. Plotkin in 1939 reported excellent results from lumbar sympathetic ganglionectomy, performed in the presence of marked ischemia of the leg 1½ hours after excision of a popliteal arteriovenous fistula. In 1940, Waugh treated an arteriovenous fistula in which the collateral circulation was so poor that sympathectomy was done before excision of the fistula. The patient experienced such symptomatic improvement that he temporarily refused further treatment for the fistula. (Subsequently, Waugh has had further recourse to sympathectomy as a preparation for obliterative procedures for arteriovenous fistulas.) In 1943 the "Military manual of traumatic surgery" (35) suggested that in cases of arteriovenous fistula, in addition to the usual methods of treatment, sympathectomy "may be of value." Subsequently a War Department "Bulletin on care of battle casualties" (48) noted that while most arteriovenous fistulas do not require emergency treatment, a certain number must have early surgical treatment in the presence of hemorrhage, impending rupture, paralysis from the pressure on the nerves near the aneurysm, or threatened gangrene. It suggests that preoperative and postoperative injections of 1 per cent solution of procaine hydrochloride to block the sympathetic ganglia or sympathectomy may be used in vascular cases to improve circulation by removing vasospasm. Recently there have been promising reports by Linton and White, Pugh, Harbison, Kirtley, Mason and Giddings (31), Shumacker and Carter and Freeman, in which there was definite evidence of stimulation of collateral circulation in chronic arteriovenous and arterial aneurysms by paravertebral block or sympathectomy. Early operation has been possible, and when there was an attendant nerve injury, repair of the nerve has been facilitated. Naide has had encouraging results from sympathetic block to supplement antitoxin and penicillin in gas gangrene infections.

This study has shown that while such a serious sequel to arteriovenous fistula as ischemic gangrene is relatively uncommon, there does exist frequently a preoperative and postoperative chronic vascular insufficiency which may be relieved by interruption of the sympathetic vasomotor control. The influence exerted by the earlier investigators in so far as depending on the time factor for the development of collateral circulation is very strong. Elkin (9) in his treatment of 106 patients who had traumatic aneurysms observed in a military hospital has not employed procedures that might be used to stimulate collateral circulation other than intermittent compression before employing obliterative operations. Many competent physicians have gone so far as to declare that attempts to improve circulation in cases of chronic arteriovenous fistula were actually contraindicated.

The results of clinical application of interruption of the sympathetic nerves performed to develop collateral circulation before opera-

tion, to prevent vasospasm at operation and to obviate chronic vascular deficiency after operation have been striking in the case of aneurysm as a group. Because of the difference of opinion among authorities as to the value of sympathetic interruption in the case of arteriovenous fistula this series of experiments was done. After the arterial collateral pattern in the presence of a chronic arteriovenous fistula had been demonstrated, the main problem was whether this abnormal portion of the vascular system could respond significantly to sympathectomy, and to a degree comparable to normal vessels. The marked rise of toe temperatures that occurred in this abnormal limb with the fistula still functioning was the answer. And since it has been demonstrated that the temperatures of the toes are in positive correlation with arterial flow, it appears that a significant increase of blood flow has been induced in the limb with a fistula by sympathectomy. The promise of favorable results that this procedure might hold for early closure of arteriovenous fistulas need only be mentioned. If blood flow may thus be increased beyond what might be expected from passage of time alone, a primary cause for delay has been removed. Another objection to early operation, the danger of infection, may be combated by the increased blood supply, plus the early, adequate use of the newer antibiotic drugs.

The beneficial effects from interruption of the sympathetic vasomotor supply to a part deprived of its normal blood supply because of an occlusive vascular lesion or because of an arteriovenous fistula have been summed up as (1) overcoming vasomotor spasm; (2) producing vasodilatation; (3) increasing blood flow through the capillary beds; (4) increasing blood volume flow through the major arteries distal to the lesion; (5) increasing the velocity of blood flow through the distal arteries; (6) increasing the size and volume flow of the vasa vasorum; (7) increasing the velocity and volume of lymph flow; (8) preventing ischemic gangrene frequently, or, where amputation is inevitable, allowing a lower level of section and a more viable stump; (9) lessening the danger from anaerobic infection; (10) allowing blood supply to depend on metabolic requirements of the tissues instead of the usual thermoregulatory mechanisms. Such an interruption may be attained with chemical block by repeated infiltration of the ganglia with procaine, by injection of absolute alcohol to prolong the effects or by surgical division as in sympathetic ganglionectomy and ramisection.

SUMMARY

The widespread belief that arteriovenous fistula is the greatest stimulus to development of collateral circulation known has led to a spirited controversy as to the rôle of sympathectomy and sympathetic block preliminary to treatment of the fistula by obliterative operation. It is the opinion of some that the vessels involved in this supposed great collateral circulation are functioning at their maximal capacity after the passage of three to six months and, therefore, should be incapable of further vasodilatation. Earlier investigators have suggested such a delay in treatment as being in itself sufficient for the development of adequate collateral circulation. The high incidence of chronic vascular deficiency, and the occasional gangrene that follows quadruple ligation and excision or obliterative endoaneurysmorrhaphy in the treatment of peripheral arteriovenous communications, however, have brought forth a promising series of clinical case reports wherein the surgeon employed some form of sympathetic denervation in the course of treatment of these lesions.

In support of this latter trend in the treatment of those patients who show evidence of vasospasm or deficient collateral circulation, we present two series of experiments. The first demonstrates by arteriography that the actual arterial collateral circulation is minor in comparison to venous response in the hind limbs of dogs in which a femoral arteriovenous fistula has been functioning for more than six months. In the second group by means of measurement of cutaneous temperatures we have followed the pattern of vascular response subsequent to formation of a traumatic arteriovenous fistula as well as the effects of lumbar sympathetic ganglionectomy on the circulation before surgical obliteration of the fistula. We have shown that such denervation is of positive value.

We wish to suggest that the abundant collateral circulation frequently referred to in

cases of arteriovenous fistula is often to a great degree spurious, being rather an enormously dilated plexus of veins, nonfunctioning as collateral circulation after obliteration of the fistula. As a result of these and other studies, it has been shown that there is a certain preexisting collateral circulatory bed present, but at low functional state and varying in efficiency according to the region involved. In contrast to most vascular abnormalities, the venous leak sets arteriovenous fistula aside as a unique condition in which delay in treatment may be of more danger from secondary cardiac and trophic changes than is warranted from the actual small increase of new arterial collateral circulation, a concept at variance with the orthodox method of treatment.

Sympathetic denervation has greater effect in opening up collateral circulation than the duration of time alone has. This was shown by a further increase of cutaneous temperatures following sympathectomy in the limbs of dogs which had had an arteriovenous fistula for seven months. Interruption of the sympathetic nerves also significantly reduces spasm of arterial branches of the involved part from (1) actual residual effects of trauma, (2) infection and (3) operative manipulation of the aneurysm. Consequently, this procedure should be considered in all cases in which collateral circulation may be inadequate or in which vasospasm from operation would be disastrous. Sympathetic denervation appears to be the means of allowing a safe early repair of arteriovenous fistulas.

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A NEW OPERATIVE TREATMENT FOR ELEPHANTIASIS

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WE shall not consider the various etiological factors of elephantiasis (Matas, 1913) but shall concern ourselves with the late stage of persistent irreversible edema with fibrosis of the subcutaneous tissues and derma in those instances or recurrent erysipeloid infections due to lymphatic obstruction.

Homans (1928), Homans and Zollinger (1929), Homans, Drinker, and Field (1934), Reichert (1926, 1927, 1930) and many others have treated this subject experimentally and clinically. It has been concluded that the most satisfactory treatment of this malady is the complete removal of the lymphatic bearing tissues especially of the legs and occasionally of the thighs. Of the various procedures used to accomplish the removal of these tissues, the Kondoleon (1912) operation of excising segments of skin and the underlying fibrous connective tissues extending down to the muscles or by the undercutting of thin skin flaps and excising the lymphatic bearing subcutaneous tissues (Sistrunk, 1927) have been used most extensively and are considered as giving the best results. These procedures are multiple, time-consuming operations requiring long hospitalization. The condition frequently recurs or is not relieved. In a true elephantiasis with progressive fibromatosis as defined by Matas, the lymphatics of the derma are involved in addition to those of the subcutaneous tissue.

This paper describes a single operation for the removal of the lymphoid bearing tissues. The procedure is simply the excision of all tissues down to the sheaths of the muscles of the thigh and leg, excepting a narrow strip covering the tibia anteriorly, and then grafting the denuded surface with thick split grafts.

Alternate procedures are illustrated in Figures 1 and 2.

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CASE REPORT

C. M., No. 275574, white male, aged 34 years was, first observed to have an enlarged left leg at the age of 2 months which was subsequently diagnosed as

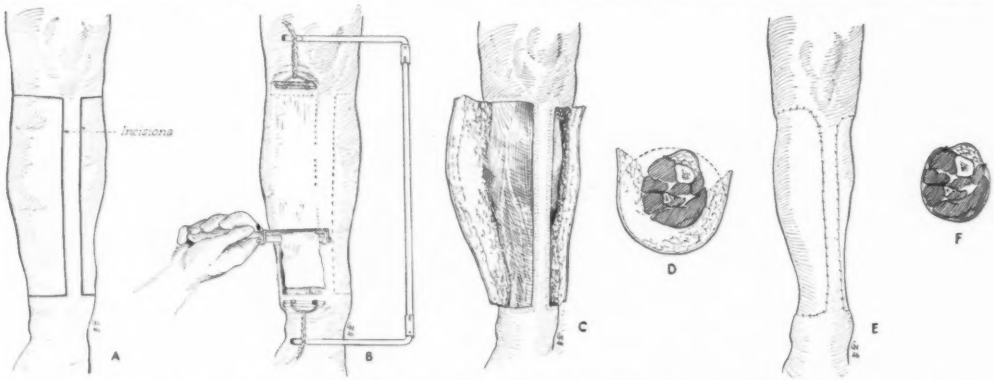

Fig. 1. One stage operation for elephantiasis. A, The incisions are outlined so as to preserve full thickness of tissue over the tibia. B, If the condition of the skin is satisfactory, thick split grafts are cut before the tissues are dissected from the operative field. Grafts are cut from the entire circumference except for the narrow strip over the tibia. C and D, show the remaining derma and subcutaneous tissues being excised down to muscle with preservation of a strip of tissues over the tibia. E and F, illustrate the situation after grafting with split skin grafts. Note: If indicated, the subcutaneous tissue over the tibia could be excised after healing has occurred.

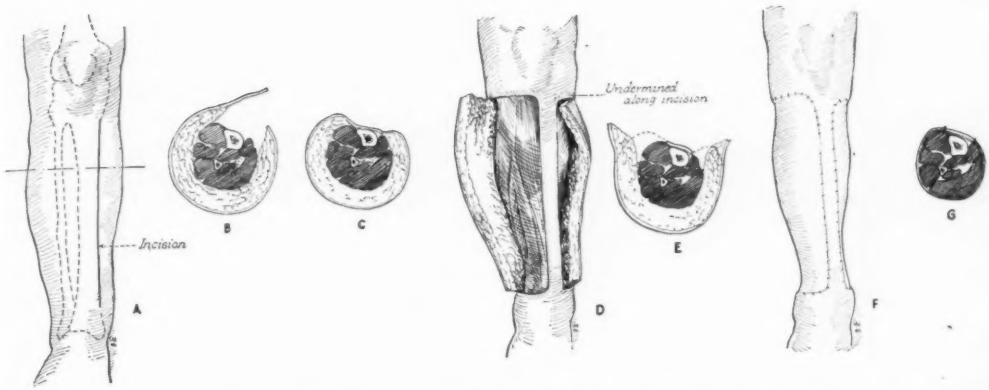

Fig. 2. An alternate two stage operative procedure. Illustrations A, B, and C show the removal of the subcutaneous tissue from the area covering the tibia. Illustrations D, E, F, and G show the completion of the operation after the flap over the tibia has healed and a new blood supply has been established.

Milroy's disease. The enlargement and edema have increased progressively with recurrent attacks of erysipeloid infection, pain, and fever. A Kondoleon operation in 1935 gave temporary improvement. Daily baths followed by sponging with 1:4000 zephiran solution as a preoperative measure succeeded in clearing the left leg of numerous small furuncles. The skin of the leg was thickened but still retained some elasticity. It was decided to cut split grafts from this surface before excising the remaining skin and subcutaneous connective tissues down to the muscle sheathes, and to use these grafts to cover the dissected area. A strip of skin and subcutaneous tissue was left to cover the tibia anteriorly (Figure 1). If the local skin is not suitable for transplantation, other donor sites should be selected. It is questionable whether the local skin should ever be used, because the lymphatic vessels of the derma are involved in elephantiasis.

The skin grafts were dressed with glycerine containing zephiran in 1:1000 concentration (Poth, 1945). Postoperative course was uncomplicated. Dressings were first changed on the twelfth postoperative day. The appearance 3 weeks and 3 months postoperatively is shown in Figures 5 and 6.

The patient has been relieved of his disability and is working as a laborer. The edema of the foot has become progressively less. A year has passed without recurrence of infection. While no supportive dressing has been worn by this patient, it is desirable to use an elastic bandage or stocking for a year to 18 months following operation.

DISCUSSION

Many patients with elephantiasis are incapacitated by the enlarged limb. The operation outlined here causes considerable disfigurement and should not be undertaken early

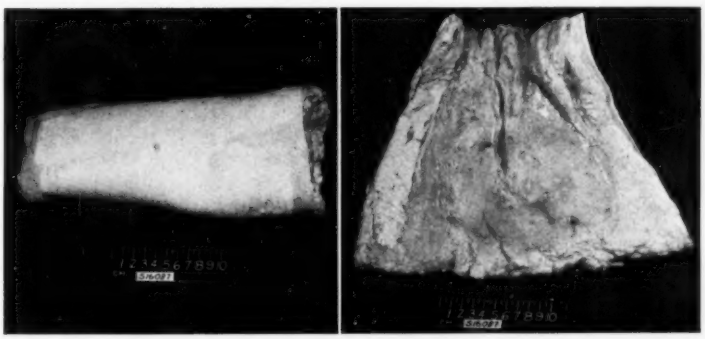

Fig. 3. The tissue excised weighed 2150 grams. A, left, shows the rolled specimen from which split grafts were cut. B, shows the deep surface.

Fig. 4. The preoperative condition of the patient, C. M., described in the text.

in a condition which might become arrested without producing a disabling elephantiasis.

It is not necessary to excise all involved tissue, because excision of the fibrosed tissues of the leg frequently results in subsidence of the enlargement of the thigh, or the abnormality of the thigh is not disabling after the size of the leg has been corrected. This operation has been applied on four occasions with good results.

This procedure will be applied to instances of extreme surgical elephantiasis of the arm following radical mastectomy (Halsted 1921).

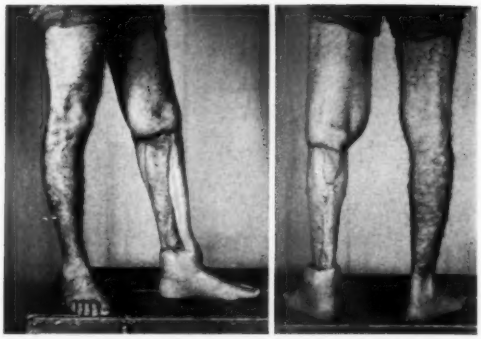

Fig. 5. The condition of the leg 3 weeks after operation. Healing is complete. Considerable edema of left foot is still present.

Fig. 6. The condition of the leg (C. M.) 3 months after operation. There is still some edema in the thickened tissues of the ankle and foot.

SUMMARY

A new operation for the treatment of elephantiasis is described together with the result of its clinical application.

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INDICATIONS FOR PORTACAVAL ANASTOMOSIS—ANALYSIS OF CASES

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THE first anastomosis to join the portal and caval system of veins was made in 1877 by Von Eck, a Russian physiologist. His operation upon dogs, anastomosing the portal vein to the vena cava, side-to-side, became widely known as the Eck fistula. Surgeons early recognized the rationale of establishing portacaval shunts for the relief of portal hypertension, and over the years from 1903 to 1914 occasional case reports appeared in the literature (3, 4).

That severe portal hypertension may cause gastrointestinal hemorrhage has long been known, but the rôle of portal hypertension in conjunction with deranged blood proteins in association with ascites is more recently better understood. In an experience covering the completion of 23 portacaval anastomoses with follow-up observations, some data having a bearing upon the selection of cases for operation have been accumulated. Since the portacaval shunt affords a rational approach to the control or amelioration of hemorrhage due to portal hypertension, I will first discuss indications for its use for this purpose.

Patients with congestive splenomegaly exhibiting Banti's syndrome, who give a history of one or more episodes of gastrointestinal bleeding, but whose liver function tests are essentially normal, may be classified as cases of portal hypertension due to extrahepatic portal block. Such patients are candidates for a portacaval shunt. In the majority of these cases the portal block is due to cavernomatous transformation or atresia of the portal vein. Since it is not feasible to anastomose the portal vein to the vena cava in the above type of case, the splenic vein to renal vein becomes the portacaval anastomosis of choice in this group. It is the surgeon's responsibility in dealing with such cases to be prepared to perform a splenorenal anastomosis before proceeding with a splenectomy. Venous pressure readings, properly taken at operation, are an indispensable aid in localizing the site of obstruction in the portal radicals. It is now an established fact that splenectomy alone for congestive splenomegaly will cure only that relatively small group of cases of thrombosis of the splenic vein in which the site of obstruction is distal to the junction of the coronary vein. In such cases venous pressure readings taken from known branches of the superior mesenteric and coronary veins are found to be normal.

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THE RÔLE OF THE PORTACAVAL SHUNT IN PORTAL CIRRHOSIS OF THE LIVER

The very fact that hemorrhage or ascites or both can occur in cirrhosis cases purely on the basis of extremely depressed liver function places a great responsibility upon the surgeon in the selection of cases for the portacaval shunt operation. I will cite cases to illustrate this point:

The first case was that of the wife of a physician whose first complaint was uterine bleeding. A dilatation and curettage revealed no cause for the bleeding and, finally during the performance of a hysterectomy, cirrhosis of the liver was discovered. Subsequent liver function and chemistry studies revealed a badly decompensated liver. The prothrombin time was markedly elevated. The patient's general condition progressively deteriorated. Some 3 months later she experienced her first episode of gastrointestinal hemorrhage. Over a period of 5 months, the patient was continuously confined in the hospital suffering repeated hematemeses occurring at monthly intervals. Finally, the patient was placed upon a high protein, high carbohydrate diet, with large doses of vitamin B complex. Gradually her appetite and strength improved. Some 4 months later, following a 6 weeks' vacation in Florida, the patient was admitted to the Presbyterian Hospital for study. The liver was found to be rather hard and enlarged. There was no ascites present. Esophagograms revealed small esophageal varices. The blood proteins

were now normal. A bromsulfalein study revealed 30 per cent retention after 30 minutes. The prothrombin time was yet moderately elevated.

There is little doubt that the hemorrhages were initiated in this case primarily by a lowered blood prothrombin due to a badly decompensated liver. The fact that the hemorrhage episodes ceased following the institution of a dietary regimen coincident with a gain in strength, weight, and appetite lends support to this idea. Accordingly, we recommended continuation of a modern medical dietary liver regimen. A recent check-up of this patient reveals her to be in excellent health. She has regained her normal weight and strength. There have been no further bleeding episodes now a year since her last hemorrhage. Whereas the liver is still enlarged, it is smaller than before. The prothrombin time has returned to normal.

If, in spite of the dietary regimen, this patient should have another gastrointestinal hemorrhage, we will recommend a portacaval shunt, for it will then be reasonably certain that portal hypertension and not a lowered prothrombin will be the responsible factor. In our opinion, it would have been an error in judgment to have attempted a portacaval shunt in this patient during the period of severely depressed liver function. We realize that uterine hemorrhage is an unusual initial symptom of cirrhosis of the liver. We cite the case to illustrate that prothrombin deficiency can cause hemorrhage independent of portal hypertension.

It is agreed that esophageal varices, the result of portal hypertension, is the usual source of hemorrhage in cases of cirrhosis of the liver. The distended varices, when subjected to the trauma of swallowing food, bleed easily. Whereas the portacaval shunt affords a rational means of reducing blood pressure in these dilated veins, the surgeon must ever keep in mind the possible rôle of a lowered prothrombin blood level in initiating hemorrhage. And, by the same token, the internist must not disregard the constant threat of the presence of esophageal varices.

Under what conditions should ascites be considered an indication for the establishment of a portacaval shunt? This question may also be best answered by citing a case, as follows:

A 55 year old woman having a long alcoholic history 1 year before began to have anorexia and weakness followed, in a few weeks, by the appearance of ascites. She was hospitalized and a thorough liver chemistry study made. The total blood proteins were low and the albumin-globulin ratio reversed. The bromsulfalein and other liver function tests revealed serious impairment of liver function. The liver was hard and greatly enlarged. Roentgenograms of the esophagus revealed no varices. The patient was placed upon a modern liver regimen and after a few weeks her appetite and strength began to improve. The ascites more gradually disappeared as her blood albumin rose. Through the summer months the patient was in excellent condition and free of ascites. In October, though her appetite, nutrition, and strength remained excellent, the patient began to develop ascites. However, a study of the blood proteins at this time revealed them to be excellent, and the liver function tests better than before. From October through December ascites became worse requiring paracenteses of increasing frequency. At this time, evidence of increased portal pressure was first observed with x-ray demonstration of esophageal varices. In the early months of the ensuing year, the patient's appetite remained good, but she could not eat adequately at any one feeding on account of the ascites. Though it was demonstrated that this patient's liver could make albumin in normal amounts, the ascitic fluid contained a fair percentage of protein and the removal of large quantities of this fluid at 5 day intervals finally began to lower her total blood proteins. Since recurrence of ascites in this case paralleled the development of evidences of severe portal hypertension, the patient's one and only chance of survival rested upon the successful accomplishment of a portacaval shunt.

The lesson to be learned from this case is that a patient with a cirrhotic liver may become doomed from a wasting ascites due to portal hypertension and at the same time have a perfectly well compensated liver. I am told by a prominent internist, who heads one of the largest medical services in the country, that the above type of wasting ascites is the predisposing factor leading to death in a considerable number of cirrhotic cases.

The modern medical and dietary regimen will often do wonders in reviving a damaged liver in varying degrees of decompensation. A sustained improvement in liver function may result. On the other hand, there is no reason necessarily to expect that such a regimen will affect fibrotic contraction of the liver by periportal fibrosis. These may be pathological processes of a predetermined course based on damage already done.

The subject of indications for portacaval shunt in cases of portal cirrhosis may be sum-

marized and clarified by classifying cases of cirrhosis in three groups as follows: Group I, cases in which ascites or a tendency to hemorrhage is based on the inability of the damaged liver to form albumin or prothrombin in adequate amounts. Portacaval anastomosis is not indicated in this group. Group II, cases of cirrhosis in which the liver function is adequate to furnish the required amount of albumin and prothrombin but as a result of fibrotic contraction and periportal fibrosis a severe degree of portal hypertension has supervened. Wasting ascites and severe hemorrhage can be controlled in this group only by the portacaval shunt. Group III, cases of cirrhosis having varying degrees of depressed liver function plus evidence of considerable elevation of the portal pressure. Such cases are candidates for the portacaval shunt operation but the question is when. It is our present policy to study the individual case with exceeding care whenever possible over a sufficient period of time to become thoroughly familiar with the behavior of the liver before bringing the case to operation. This is usually possible even in patients who have been subject to recurring hemorrhages. The idea is to improve liver function to its maximum employing a comprehensive liver regimen energetically applied for as long a period as necessary.

DISCUSSION

The portacaval shunt operation is indicated and affords a chance of ultimate survival for cases of Banti's syndrome with extrahepatic portal block cases in which there is hypertension in the coronary or portal veins.

The portacaval shunt has an equally important rôle in the treatment of portal hypertension due to cirrhosis of the liver. But, its application must be decided on the basis of portal hypertension being the primary cause of hemorrhage or ascites in the individual case.

ANALYSIS OF CASES

The portacaval shunt operation has been completed in 23 cases. There have been 4 postoperative deaths.

Hemorrhage from a sizable collateral vessel discovered at the conclusion of an anastomosis of the portal vein to vena cava accounted for death in a case of cirrhosis of the liver. One cirrhosis patient died of cholemia 4 days following the establishment of a splenorenal shunt. Another cirrhotic patient died also of liver failure 6 days following the establishment of a portal vein to vena cava anastomosis. The fourth death resulted from mesenteric thrombosis occurring on the 14th day following a splenorenal anastomosis. The first death was the result of technical error. Death from liver failure in the 2 cirrhotic patients involves essentially errors in judgment in the selection of cases. Whereas mesenteric thrombosis is in the lap of the gods!

Patients have been explored in whom it was not feasible to accomplish a shunt operation. The majority of these patients had been subjected to a previous splenectomy. Of the 23 cases in which portacaval shunts were completed, there were 15 patients who had anastomosis of the splenic vein to the renal vein following splenectomy and left nephrectomy. One of these patients had had a splenectomy at a previous operation. In one other post-splenectomy bleeder it was possible to anastomose the stump of the splenic vein to the vena cava, end-to-side, by suture.

Anastomosis of the portal vein to the vena cava, end-to-side, was carried out seven times. A 12 millimeter vitallium tube was used four times (1), a 10 millimeter once; an 8 millimeter vein-lined tube once and suture anastomosis once.

Seventeen of the 19 patients surviving operation have a follow-up exceeding 6 months. Two deaths have occurred: one, a child having portal cirrhosis, died some 2 years 4 months postoperatively of uremia due to polycystic disease of the kidney; the second case, a man with bad portal cirrhosis, died 1 year following operation, of cholemia. A necropsy examination was made in each case. In the child, the splenorenal shunt had become occluded. This outcome was not unexpected because at operation in this, our first case, there was considerable angulation of the splenic vein over the funnel edge of the vitallium tube. The splenorenal anastomosis in the second case was found to be patent.

Five additional patients with bad cirrhosis of the liver have been followed (2 cases, 2

Fig. 1. Case 536889. a, left, Infrared photograph. Note distention of abdomen with ascites, umbilical hernia and the presence of superficial collateral veins. b, Same patient 5 months after the establishment of a splenorenal shunt. The ascites has completely disappeared.

years each; 3 cases 1½ years each). All, for the most part, have done satisfactorily, considering their preoperative status. All of the patients are active and 4 of the 5 are working. There was delay in disappearance of ascites following operation in 1, a minor bleeding episode in another.

I should like to discuss in more detail a sixth case, a patient with extrahepatic portal vein obstruction and biliary cirrhosis who has been followed now 2 years since the establishment of a splenorenal shunt.

Case 536889. The question of performing a portacaval shunt procedure on this 46 year old man arose during an admission for hematemesis in November, 1944. This was his 10th admission to the Presbyterian Hospital over a 7 year period.

His initial troubles began with an impacted gall stone causing cicatricial stenosis of the distal common duct and fibrotic pancreatitis. The latter caused partial obstruction of the duodenum and finally obstruction of the portal vein. As corrective measures, a gastroenterostomy and a cohlecystjejunostomy were performed. Some 5 years later, because of recurring attacks of jaundice, cholangitis, and a persistently high alkaline phosphatase, an operation connecting the proximal end of the common duct to the pylorus using a vitallium tube was performed. In spite of this procedure over the next 2 years this patient's health continued to deteriorate. There was progressive loss of strength, appetite, and weight. The episodes of cholangitis recurred in spite of long periods of therapy with sulfadiazine. The liver remained large with laboratory evidence of progressive cirrhosis. The spleen became more and more enlarged *pari passu* with the development of prominent superficial veins over the abdomen. Finally, esophagograms revealed the presence of varices. Ascites supervened. Over an 8 month period prior to this admission the patient suffered five episodes of severe gastrointestinal hemorrhage.

On November 30, 1944, a splenorenal portacaval shunt employing a vein graft with two 5 millimeter vitallium tubes was carried out. Following the above procedure there was a reduction in size of the superficial abdominal veins. The ascites, which had been present for some 8 months before operation, gradually disappeared. Over the first 10½ months following the establishment of the portacaval shunt, the patient gained 22 pounds. His appetite and digestion were excellent. He was working daily until October 12, 1945, when he caught cold. Following a severe coughing attack, the patient had abdominal pain and 2 days later the patient passed 2 or 3 tarry stools. This episode cleared promptly, however,

with a rapid return of strength and appetite. Some 3 months later, in January, 1946, the patient began to have gas on the stomach with upper abdominal pain. The pain was relieved temporarily by eating or the ingestion of alkalis. One month later (February, 1946), the patient again passed a few tarry stools. He was hospitalized for a short while during which he recovered his strength nicely but continued upon discharge to suffer daily from intermittent abdominal pain. A month later (March 25, 1946), the patient was admitted for his third episode of tarry stools since the portacaval shunt operation. Because of the persistence of intermittent attacks of abdominal pain favorably affected by the ingestion of food or alkali, the presence of a marginal ulcer was considered but not proved by x-ray. Nevertheless, this patient's stools did not become guaiac negative until after the administration of amphojel therapy during which time the attacks of abdominal pain entirely disappeared. The patient has continued free of digestive symptoms or pain now some 6 months during which there has been no recurrence of bleeding from the gastrointestinal tract.

See Figure 1, infrared photographs, a, before operation, b, 5 months after operation.

This patient has had three episodes of gastrointestinal bleeding since operation. Three possible causal factors may be discussed in explaining the recurrence of bleeding:

1. Occlusion of the anastomosis: a femoral vein graft mounting a 5 millimeter vitallium tube on either end was employed to bridge the splenic and renal veins in this case—a technique which combined what we now consider 2 objectionable features, namely, the employment of a vein graft and the use of vitallium tubes of a diameter undesirably small. On the other hand, there is an extremely good argument against occlusion of the anastomosis as being the cause of the recurrence of bleeding in this case.

2. Hemorrhage from a marginal ulcer at an old gastroenterostomy site: Against this as a source of bleeding was the failure to demonstrate a marginal ulcer in this case by x-ray. It is of extreme interest, however, that the first bleeding episode to occur following the establishment of the portacaval shunt manifested itself in tarry stools 2 days after the onset of epigastric pain. The patient stated that at the time he had a coryza and a productive cough—the pain following a coughing episode. Three months later the epigastric pain recurred accompanied by the eructation of gas. The ingestion of food would relieve the pain temporarily. These new symptoms persisted and during the next 3 months occurred the second and third bleeding episodes. The persistence of guaiac positive stools and abdominal pain was protracted until the institution of amphojel therapy following which the pain ceased and the stools rapidly became guaiac negative. The patient's digestion and appetite improved steadily and now 6 months later the patient has gained 18 pounds and his stools remain guaiac negative.

3. A third possible explanation for the bleeding in this case is a logical one, namely: the rather small (5 mm.) vitallium tubes employed may not handle a volume of blood adequate to lower pressure in the portal radicals sufficiently under conditions of sudden strain or possibly in the presence of mucosal ulceration. One look at the size of the collateral veins over this man's abdomen lends distinct credence to this explanation.

Though a splenorenal shunt be not adequate in size to afford total protection against the occurrence of bleeding, that does not mean it will not do yeoman service in lessening the number and severity of attacks—a logical explanation of the clinical behavior in this case.

Our experimental evidence and clinical experience indicate that if a blood vessel anastomosis remains patent up to 60 days following operation it is extremely likely to remain open permanently. Here is a man who, for 8 months prior to operation had ascites requiring paracentesis. During this period there were 5 episodes of severe gastrointestinal hemorrhage including hematemesis. For a month prior to operation the patient's condition was extremely precarious due to persistent gastrointestinal bleeding. A splenorenal shunt was established at this point. Following operation there was marked clinical improvement. The ascites disappeared and there was a gradual gain in weight of 22 pounds.

It is logical to conclude that the patency of the anastomosis accounted for the disappearance of ascites in this case. The presence of persistent ascites for 8 months prior to operation had been conceded by all to be on the basis of portal vein compression due to a fibrosing pancreatitis. Whereas the patient did have biliary cirrhosis, there was never at

TABLE I.—PROTEINS

Name		Preoperative			Postoperative		
		Total proteins	Albumin	Globulin	Total proteins	Albumin	Globulin
1. Duncan 27, M 767171	Esophageal varices Splenorenal shunt	6.6	2.9	3.7	7.1	3.6	3.9
2. Box 47, F 777262	Esophageal varices Eck fistula	7.8 8.1 8.0	4.3 3.9 4.1	3.5 4.2 3.9	5.6 6.6 6.1	3.4 4.1 3.8	2.2 2.5 2.4
3. Pahuci 5, F	Ascites. Esophageal varices. Splenorenal shunt	8.2	4.5	3.7	7.4 7.2 7.2 7.3	3.5 3.7 4.1 3.8	3.9 3.5 3.1 3.5
4. Scheingarten 28, M 557450	Esophageal varices. Eck fistula. Vein graft.	8.5	3.3	5.2	6.9 7.1 7.9 8.8 6.2 7.4	2.6 2.4 2.2 (1.5) 2.2	2.3 4.7 5.7 6.3 4.7 5.1
5. Cocozelo 42, M 754188	Ascites. Esophageal varices. Splenorenal shunt	7.5	3.5	4.0	6.2 6.8 6.5	2.5 2.6 2.6	3.7 4.2 3.9
6. Mooney 55, M 536889	Esophageal varices. Splenorenal shunt.	5.7 7.1 6.4	3.2 3.8 3.5	2.5 3.3 2.9	6.4 7.2 5.8 6.5	3.7 4.1 3.1 3.6	2.7 3.1 2.7 2.8
7. Long 49, M 783972	Ascites. Eck fistula	5.3	2.3	3.0	5.9 5.4 5.7	3.6 2.6 3.1	2.3 2.8 2.6
8. Iacoletti 58, M 784905	Ascites. Eck fistula	5.2	2.9	2.3	4.5 4.9 4.7 5.0 5.0 5.0 6.2 5.0	2.5 2.3 2.9 1.9 2.0 2.2 3.0 2.4	2.0 2.4 2.0 3.1 3.0 2.8 3.2 2.6

NOTE: All cases of cirrhosis of the liver.

any time evidence of decompensation of the liver. Furthermore, up until the time of disappearance of the ascites following the establishment of the portacaval shunt, the patient was not on a liver dietary regimen. In view of the above fact, if the bleeding episode which occurred 10½ months after operation in this man had been due to a sudden closure of the splenorenal shunt, one would have expected a prompt return of the ascites. In fact, in a very recent case in which thrombotic occlusion did take place, the prompt occurrence of ascites antedated the appearance of esophageal bleeding by 2 weeks.

It seems reasonable that this man's splenorenal shunt may be open but not of a size adequate to shunt enough blood to afford complete protection against hemorrhage. After all, he has had only three episodes of gastrointestinal hemorrhage in a 24 months' postoperative period compared to 5 attacks over an 8 months' period before operation. He is free of ascites, and working.

We do not have, as yet, enough follow-up data on portal pressures before and after opening portacaval shunts to predicate what pressure level will afford absolute protection against hemorrhage. However, we do have data upon portal pressures to indicate that the splenic vein may not always be of adequate size to afford a shunt sufficiently large to protect against episodes of hemorrhage. As a possible corollary to the importance of the size of the shunt our follow-up has not so far been complicated by hemorrhage in those cases in which direct anastomoses of the portal

TABLE II.—BROMSULFALEIN LIVER FUNCTION TEST

Percentage of Dye Retained After 30 Minutes

Name	Preoperative Per cent	Postoperative Per cent
Pahuci 090444	10	5 10 8
Duncan 767177	70	38
Cocozelo 7541188	60 (S.B. 1.5 mgm.%)	65 (S.B. 2.5 mgm.%)
Box 777262	45	10 30 20
Scheingarten 557450	42	40
Mooney 536889	20 (S.B. 3.5 mgm.%)	22 (S.B. 1.0 mgm.%) 25 35 27
Iacoletti 784905	35 (S.B. 4 mgm.%)	35 (S.B. 3 mgm.%) 20 (S.B. 3 mgm.%) 27 (S.B. 3 mgm.%) 61 No jaundice 55 39

NOTE: An elevation of the serum bilirubin may have affected the accuracy of the tests in 3 cases.

TABLE III.—HIPPURIC ACID LIVER FUNCTION TEST

(Normal Excretion One or More Grams Per Hour

Name	Preoperative	Postoperative
Long 783972	0.62 grams 1 hr.	0.82 grams 1 hr.
Scheingarten 557450	0.8 grams 1 hr.	1.1 grams 1 hr. 1.5 grams 1 hr. 1.3 grams 1 hr.

Cephalin flocculation test

	Preoperative	Postoperative
1.	4+	0
2.	3+	2+ .5 1.25+
3.	4+	0
4.	1+ 1+	0 0 0 0
5.	3+	2+ 3+ 0 2+
	Iacoletti negative 784905	1.75+ 4+

Prothrombin time

In those cases with elevated prothrombin times, the times usually have returned to normal.

vein to the vena cava have been successfully completed.

The variations in size of the splenic vein and thereby the splenorenal shunt as it affects portal pressures is illustrated by the cases outlined in Table IV.

Considering 100 millimeters of water as normal for portal pressure, the above figures show what may be expected from an average splenorenal shunt.

Our data on portal pressures are not statistically adequate. In 6 cases of Banti's syndrome the portal pressure averaged 332 millimeters of water. In 7 cases of portal cirrhosis the pressures averaged 294 millimeters of water. Multiple episodes of gastrointestinal hemorrhage had occurred in all of the Banti's group, whereas gastrointestinal bleeding had occurred in only 2 of the 7 cirrhosis cases. In one of these, in which the bleeding episodes had been severe, the portal pressure measured 330 millimeters of water.

Of 19 patients surviving the successful completion of portacaval shunts one or more episodes of gastrointestinal bleeding has occurred in 8 cases. Two of the 8 patients are now dead. One, a 5 year old child upon whom we did a splenorenal anastomosis, died some 2 years later of uremia due to polycystic disease of the kidney. At necropsy the anastomosis was observed to be occluded. This child had several episodes of bleeding.

The second patient died in cholemia one year after the establishment of a splenorenal shunt. At necropsy the anastomosis was observed to be patent. This man's episode of gastrointestinal bleeding occurred during his

TABLE IV.—VARIATIONS IN SIZE OF SPLENIC VEIN

Case No.	Age	Sex	Portal pressure mm. water before anastomosis	Vitallium tube diameter in mm.	Portal pressure mm. water anastomosis open
817184	26	M	315	8	180
819382	11	M	330	8	180
756752	15	F	310	7	190
7541188	38	M	400	8	240

terminal illness from liver failure. Whereas it seems likely that a low blood prothrombin level may have contributed to the initiation of hemorrhage, it must be remembered that this patient still had a portal pressure of 240 millimeters of water following opening of the shunt. Before operation the portal pressure was 400 millimeters of water—the highest pressure we have yet recorded on a case of cirrhosis. Though this patient's ascites cleared following operation, his jaundice persisted. His terminal illness was ushered in by a high fever from what appeared to be an upper respiratory infection. It is only fair to state at this point, however, that following the establishment of a splenorenal shunt, this man's appetite, strength, and weight improved. He was able to return, for part time work, to his job as a barber.

The above case proves that a splenorenal shunt, though patent, may not be of a size adequate to shunt an amount of blood sufficient under all conditions to afford absolute protection against future hemorrhage. Three additional cases over a 2 year follow-up period have shown such marked overall clinical improvement following the portacaval shunt operation as to justify including them in the above classification.

One of the cases has already been discussed in detail. One case, a girl of 15 years, having Banti's syndrome with extrahepatic portal block was found to have a portal pressure of 310 millimeters of water. Following the opening of a splenorenal anastomosis the portal pressure receded to 190 millimeters of water. This patient gained strength and weight following operation, but over a 2½ year (30 month) follow-up period she has had three episodes of gastrointestinal bleeding. Two of these hemorrhages were comparatively trivial to the attacks which came regularly at 6 month intervals before operation.

A third case, a cirrhotic who gave a long past history of hematemesis, was operated upon following a month's seizure of hemorrhage, during which the stools failed to become guaiac negative. Following the establishment of a portacaval shunt, this man's general condition improved markedly. His jaundice gradually improved as well as his liver function tests. A few months after operation, the patient returned to his job and has been working ever since. Over a 2 year follow-up period this man has had one comparatively minor bleeding episode consisting of 2 or 3 tarry stools.

Finally, there are 3 cases in which the evidence points to closure of the portacaval anastomoses. All 3 cases have Banti's syndrome with a past history of frequent episodes of gastrointestinal bleeding including hematemesis. In 1 case, that of a 15 year old girl, who 4 years previously had had a splenectomy, an anastomosis was effected by suture of the stump of the splenic vein to one branch of the left renal vein. To the other branch of the renal vein (following nephrectomy) the proximal stump of the inferior mesenteric vein was anastomosed employing a 5 millimeter vitallium tube. Thrombotic occlusion of the anastomoses was heralded by the sudden appearance of ascites on the seventh postoperative day. Some 2 weeks later the patient had an attack of hematemesis. The bifurcated renal branches were rather small in this case and in retrospect it would possibly have been better judgment to have been satisfied with one anastomosis.

The second case was that of an 8 year old boy, who one year previously had had a splenectomy. The boy had Banti's syndrome complicated by bronchiectasis. During the year following splenectomy the boy suffered 5 episodes of severe gastrointestinal hemorrhage including hematemesis. The proximal stump of the splenic vein was anastomosed to the vena cava by suture, end-to-side. During a year following this procedure, as presumptive evidence of closure of the anastomosis, the hemorrhages have recurred with equal frequency and severity.

Finally, in a child 3 years of age an end-to-end suture of the splenic vein to the renal vein has failed to lessen the tendency to hemorrhage over a year's follow-up period.

SUMMARY

In presenting the rationale of the portacaval shunt for the relief of portal hypertension, special stress is placed upon the selection of cases.

The procedure is presented as the one hope of relief for those cases with Banti's syndrome who have essentially normal livers but present the problem of control of gastrointestinal hemorrhage.

The importance of exercising extreme care and judgment in the selection of cases of cirrhosis for operation and the reasons thereof are discussed.

An analysis of 23 cases having portacaval anastomosis was presented.

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ANOMALIES OF THE PULMONARY VEINS

Their Surgical Significance

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THE reports of anomalies of the pulmonary veins are appearing more frequently in the medical literature. In the past all descriptions and case reports have come from autopsy material or from studies made in the anatomic laboratory. This article will describe and discuss anomalies of the pulmonary veins found at the time surgical operations were being performed upon the lungs.

Brody made a review of the literature and in 1942 presented an excellent discussion of the subject. The final study included 106 patients. Since 1942 seven different authors have reported 14 additional cases (3,4,7,8,10, 11,12). Brody classified the anomalous venous drainage from the lungs as (1) total drainage into the right atrium or its tributaries, 36 per cent, and (2) incomplete drainage into the right atrium or its tributaries, 64 per cent. When the venous drainage from the lungs into the right atrium or its tributaries is incomplete, the most common site for drainage in order of frequency is the superior vena cava, right atrium, and the left innominate vein. The right pulmonary vein is anomalous in its drainage twice as frequently as the left.

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Anomalous pulmonary veins have been described as draining into the following: superior vena cava, right atrium, left innominate vein, coronary sinus, inferior vena cava, azygos vein, left subclavian vein, portal vein, and persistent left superior vena cava.

It has been suggested that if less than 50 per cent of the pulmonary blood is abnormally shunted into the major venous system or into the right side of the heart, the patient is unlikely to develop cardiac decompensation. Such an assumption is based upon a normal heart. Hughes and Rumore were the first to give actual figures that might indicate the quantity of pulmonary blood that flows abnormally into the major venous system from an anomalous pulmonary vein. Both of the patients they described died of cardiac failure and both had rheumatic heart disease. By comparison of the cross-sectional area of the anomalous veins with the cross-sectional area of the normal pulmonary veins, they calculated that in one patient 26 per cent and in another 20.1 per cent of the pulmonary blood was shunted into the major venous system. It is difficult to calculate the effects of this additional effort upon the already injured heart. Conant and Kurland described a patient who tolerated extensive tuberculosis in the left lung but died rapidly when the right lung became infected. At autopsy it was found that

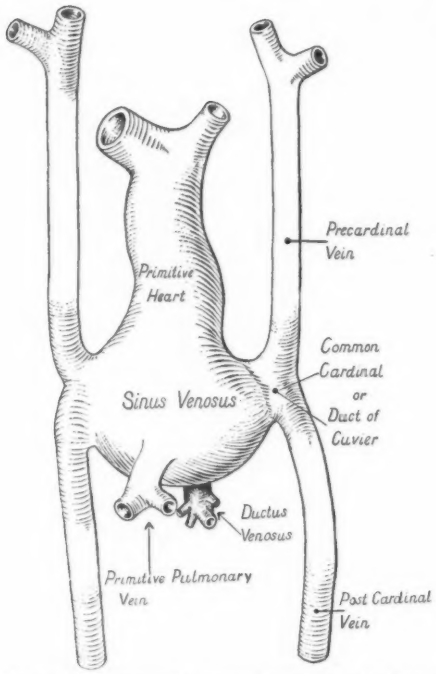

Fig. 1. A diagrammatic conception of the primitive venous system viewed from the dorsal aspect. The primitive pulmonary vein enters the dorsal wall of the sinus venosus. This conception was accepted by the early embryologists.

the blood from the left lung drained anomalously and completely into the left innominate vein. Disease of the nonfunctioning lung caused little embarrassment to the patient, but disease of the functioning lung was rapidly fatal. Thus, the physiologic effect of pulmonary blood shunted into the major venous system will be influenced by disease in the functioning lung or by disease of the heart.

The seemingly wide and unrelated variations that occur in pulmonary venous anomalies have been studied from the embryologic point of view in an endeavor to simplify and correlate the anomalies encountered. Brown reviewed the research that had been done on the development of the pulmonary veins and wrote it is evident that "(1) The anlage of the vein and its connections with sinus venosus has not been described in detail, and (2) the method by which the vein changes its orifice in the center of the sinus venosus for one in that position of the sinus which lies to the left of the left sinus valve has not been considered. In addition, the general relation which the pulmonary venous system bears to the systemic has been entirely neglected in the study of the embryology of the vein." In the 4.5 millimeter cat embryo he reported "At this stage the pulmonary vein exists as a single vessel having two main vascular connections, (1) ventrally a single rounded orifice in the sinus venosus (Fig. 1), and (2) dorsally a connection with that portion of the splanchnic plexus which is pushed forward by the growing pulmonary anlage which it joins at the ventral pole of the lung bud." Thus, the pulmonary venous plexus through the splanchnic venous plexus is connected with the primitive major venous system by the way of both the precardinal and postcardinal veins. In the 6.5 to 7 millimeter embryo he further related "The sinus venosus with the exception of the openings of the cornua has been incorporated into the auricle. The right valve of the sinus is very prominent and is continued into the septum spurium which has shifted to the left and fused with the septum superius. The left valve of the sinus has likewise shifted to the left and its cephalic extremity on the dorsal wall of the auricle has fused with the dorsal caudal portion of the septum superius. As a result of the latter shift the orifice of the pulmonary vein has preceded the left valve of the sinus, passed under the septum superius and now empties into the left auricle having both septum superius and left valve of the sinus or, in other words, the interauricular septum on the right." This view is no longer considered to be true in human development. It is thought that the venous plexus covering the primitive lung bud is probably a development from the splanchnic venous plexus (Fig. 2). The pulmonary venous plexus is gathered together into a common pulmonary vein that joins directly and definitively with the left auricle (6,16). Patten in describing human embryology said "Phylogenitically the lungs are relatively new structures. It is not surprising, therefore, that we find the pulmonary veins arising independently and not by the conversion of old vascular channels. They originate as vessels which drain the various branches of

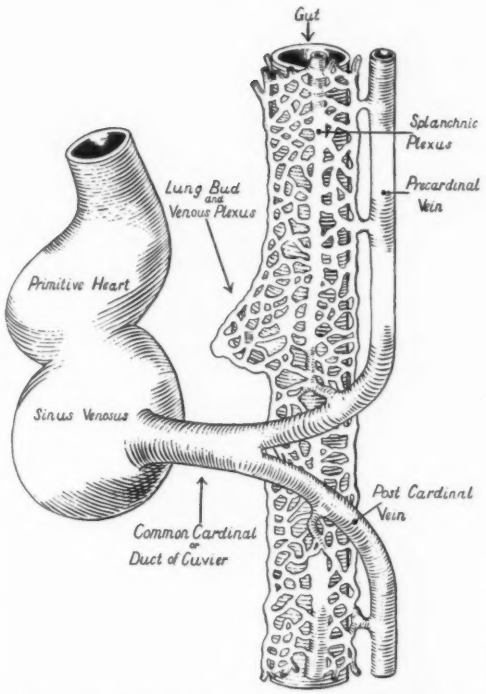

Fig. 2. A lateral view diagrammatically representing the primitive venous system and the lung bud and its venous plexus. The primitive pulmonary plexus is an outgrowth from the primitive splanchnic venous plexus. The primitive splanchnic venous plexus communicates with the precardinal and postcardinal veins. The pulmonary vein arising from the primitive pulmonary venous plexus will join directly and definitively with the left atrium. This conception of development for the most part is accepted by contemporary embryologists.

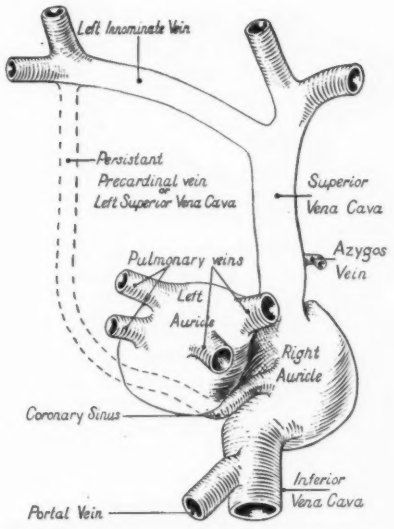

Fig. 3. With the exception of the right and left atria, the diagram presents the normal adult structures arising from the primitive venous system. It is viewed from the posterior aspect. If there is a left superior vena cava it is the result of a persistence of the left precardinal vein. The normal coronary sinus is the normal remains of the old precardinal vein on the left side. If the pulmonary blood is drained abnormally into the right atrium or its tributaries it will drain into one of the structures indicated on this diagram.

the lung bud and converge into a common trunk entering the left atrium dorsally. In the growth of the heart this trunk vessel is gradually absorbed into the atrial wall until usually 4 of its original branches come to open into the left atrium as the pulmonary veins of the adult. Less than the usual amount of resorption of the primitive common pulmonary vein not infrequently results in the pulmonary veins from the right and the left lungs entering the left atrium as single instead of the usual paired vessels (Fig. 4)." In continuation of the discussion Patten made the statement, "Occasionally startling anomalous connections of the pulmonary veins are seen, such as the entrance of one of them into the superior vena cava, the left innominate or the azygos. Such conditions are explicable only on the basis of exceedingly early embryonic stages in which the developing foregut, trachea, and lung buds are supplied by a common plexus of small channels which thread in all directions through the loose mesenchyme and communicate with the primitive cardinal veins freely in many places (Fig. 2). With the enlargement of certain channels in the primordial vascular bed to form pulmonary veins leading to the left atrium, the primitive connections with the cardinal veins ordinarily disappear. The unusually strong development of some one of these early channels and its retention by the adult derivative of the particular part of the cardinal system involved is behind the occurrence of these abnormal pulmonary connections."

The primitive venous system consisting of the cardinal veins and sinus venosus give rise

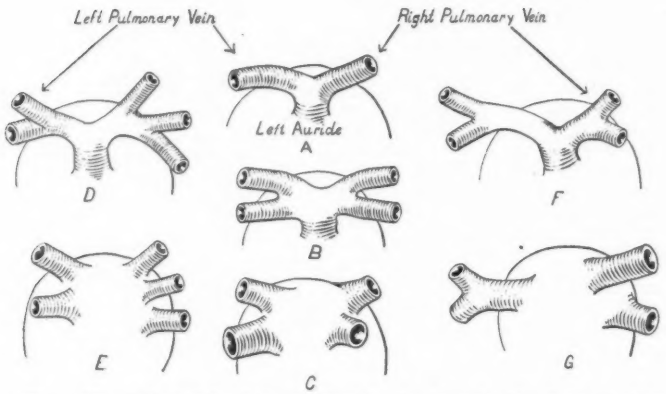

Fig. 4. The method of development of an abnormal number of pulmonary veins entering the left atrium is indicated by the diagrams A to G. The dorsal aspect is presented. The primitive pulmonary vein enters the left atrium as a single venous trunk. The primitive single venous trunk is divided into a right and a left pulmonary vein, A; the right and left pulmonary veins are divided into two veins, B. There is resorption of the venous trunks into the wall of the left atrium until in the normal adult atrium four pulmonary veins open separately into the posterior aspect of the atrium, C. If the right pulmonary vein divides into three branches, D, one for each lobe, close to the atrium they will be resorbed into the atrial wall, thus giving rise to three separate openings on the right side, E. If the left pulmonary vein divides into two branches at a greater than normal distance from the atrial wall, F, they will not be taken up into the atrium and thus only one orifice will open into the atrium on the left, G.

in the adult to the right and left innominate veins, the coronary sinus, the azygos vein, the superior vena cava, the portion of the inferior vena cava adjacent to the atrium, a part of the right atrium, and a portion of the portal vein adjacent to the liver. Abnormalities in the persistence of the cardinal veins may give rise in the adult to abnormal azygos veins and to a left superior vena cava (13,14). When there is anomalous drainage of blood from the lungs, according to all past reports, it has drained into one of the structures above named. Abnormal sites of drainage of pulmonary blood at first glance seem unpredictable but actually they are rather normal from the embryologic point of view. This blood will always drain into some structure originating from the primitive venous system (Fig. 3).

If the early pulmonary veins once drained into the sinus venosus an abnormal shift of its final drainage point could easily account for an abnormal pulmonary drainage into any of the structures originating from the primitive venous system and, especially, the emptying of pulmonary veins into the right atrium. Should the pulmonary veins originate from the splanchnic venous plexus (Fig. 2) and then drain first and definitively into the left atrium, certain early connections of the splanchnic venous plexus with the cardinal venous system may persist and thus account for the anomalous drainage of pulmonary blood into any part of the major venous system originating from the primitive venous system. If there is failure of junction of the early pulmonary vein with the left atrium then all blood from the lungs must find an anomalous pathway for drainage. Thus, all anomalies that have been described can be accounted for whether one accepts the old or the new embryologic theory of pulmonary vein development (Fig. 1, 2, 3, and 4).

Embryologists seem to agree upon the essential method of development of multiple openings of the pulmonary vein into the left atrium. The method is described adequately in the quotation from Patten. The various anomalous openings and their method of development have been indicated by the diagrams in Figure 4.

In the last 3 years pulmonary venous anomalies have been recognized by the author at the operating table. While undergoing pneumonectomy 3 patients were found to have only one pulmonary vein on the left side. Thus, to remove the left lung only one pulmonary vein was ligated. In each patient the single vein was ligated as it entered the pericardium. During pneumonectomy 2 other patients presented 3 pulmonary veins on the right side, or an individual vein for each lobe of the lung on the right side. Upon removal of the lung in these 2 patients 3 veins were ligated as they entered the pericardium. In 1 patient where the right lung was removed for tuberculosis the pulmonary vein from the upper lobe of the right lung drained into the inferior part of the superior vena cava. The pulmonary vein from the middle and lower lobes of the right lung drained into the left auricle. While doing a closed intrapleural pneumonolysis on the left side a pulmonary vein from the upper lobe of the left lung was found draining into the left innominate vein. Since this lung was not removed and since it was viewed through a thoracoscope, the interpretation may be erroneous.

When the various anomalies of the pulmonary veins are understood it is reasonable to expect that they will be recognized with greater frequency at the operating table. It is evident that these anomalies are of considerable surgical importance. This importance is mitigated by rarity and enhanced by common occurrence.

Pulmonary vein anomalies can be classified into two groups: (1) an abnormal number of pulmonary veins emptying into the left atrium; (2) abnormal drainage of the pulmonary veins; (a) partial drainage into the right atrium or its tributaries, (b) total drainage into the right atrium or its tributaries.

In performing a lobectomy by means of the individual ligation technique, the presence of more than a single pulmonary vein must be demonstrated in order to avoid devitalizing the whole lung. When 3 veins are present on the right side the ligation of the vein draining the lobe is facilitated. The variable number of veins that may be found draining the lung is well recognized and described in the standard textbooks of anatomy (9,5). If the pulmonary veins were inspected inside the pericardium it seems reasonable to expect that a single pulmonary vein on either side would be of more common occurrence.

It has been recognized that the drainage of pulmonary blood into the major venous system or into the right atrium is a burden upon the heart. The thoracic surgeon endeavors to conserve healthy lung tissue when resection of the lung is necessary. It is important to recognize pulmonary venous anomalies when the thorax is open, since the removal of such a lobe of the lung would be beneficial to the patient by eliminating the burden placed upon the heart. Lobectomy of the lower lobe is more common than lobectomy of the upper lobe of the lung. If the pulmonary vein of an upper lobe drains into the major venous system and the normally draining lower lobe is removed, it will increase the relative percentage of pulmonary blood drained into the major venous system. Accordingly, it will increase the cardiac burden and should be removed. The most common anomalous pulmonary venous drainage is the drainage of the pulmonary vein from the upper lobe of the right lung into the superior vena cava.

For the thoracic surgeon it is frightening to contemplate the possibility of removing one lung only to find that the other lung drained its blood into the major venous system, as in the patient described by Conant and Kurland. Fortunately, the drainage of one lung into the major venous system is uncommon. Judged from case reports it occurs about as often as drainage of the total pulmonary blood into the right atrium or its tributaries. Actually, 31 such cases have been reported.

In the past a diagnosis of total drainage of pulmonary venous blood into the right atrium or its tributaries has not been made before death. In such patients death usually coincides with the closure of the foramen ovale. It is not unreasonable to believe that some day the condition will be diagnosed before death. If that were possible it would be interesting to speculate upon an operative attack: the interatrial septum might be removed or a major pulmonary vein could be anastomosed to the left atrium.

CONCLUSIONS

1. The anomalous drainage of pulmonary blood is being recognized with increasing frequency.

2. When there is anomalous drainage of blood from the lung it drains into some structure arising from the primitive venous system.

3. An anomalous number of pulmonary veins draining into the left atrium is not uncommon and is recognized by the standard textbooks of anatomy.

4. In the individual ligation technique for lobectomy of the lung, it is important to demonstrate the presence of more than one pulmonary vein if devitalization of the whole lung is to be avoided.

5. If there is anomalous drainage of pulmonary blood into the major venous system, the patient will be benefited by removal of the portion of lung thus drained.

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THE USE OF VASODILATATION IN THE TREATMENT OF VENOUS THROMBOSIS

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THE rationale for vasodilatation obtained by sympathetic block in the treatment of venous thrombosis is that in true thrombophlebitis, because of the irritative lesion within the vein, impulses are set up and carried over the sympathetic nervous system to the arterioles and venules, resulting in severe spasm. As we have emphasized previously (10–15), it is imperative to differentiate between two types of venous thrombosis, one in which the thrombus is associated with, and is dependent upon, an inflammation of the vein wall; i.e., thrombophlebitis, and another in which the clot is a coagulation thrombus and occurs not as a result of an inflammatory process in the vein wall, but because of two other factors: a predisposing one, consisting of increased coagulability of the blood caused by tissue damage, and another, a precipitating one, consisting of circulatory stasis which determines the site of the thrombus. These two types of venous thrombosis must be differentiated not only from an etiologic standpoint, but also from the standpoint of their clinical manifestations, their prognosis, and their treatment. Pathologically, the clot in thrombophlebitis is a white or mixed thrombus. It is firmly attached to the vein wall and will not become detached. For this reason, there is little or no danger of embolism except in the rare instance in which there is suppuration and in which, because of liquefaction of the clot, infected emboli can become detached. On the other hand, in phlebothrombosis the clot is a red, or coagulation, thrombus. It is not firmly attached to the vein wall and can become detached easily. The patient with phlebothrombosis is a potential fatality and, although the symptoms are minimal or lacking, there is great urgency for radical therapy. The symptomatologies of the two conditions are entirely different. The patient with thrombophlebitis has definite symptoms which vary according to the location, whether the deep or the superficial veins are involved. In femoroiliac thrombophlebitis, which is the most frequent type and which is a typical example of phlegmasia alba dolens, the symptoms are maximal. There is pain and fever, and the extremity is swollen, white, and cold. The significance of the paradox, the whiteness and coldness of an extremity in an individual with pyrexia and whose surface temperature elsewhere is increased, was not previously appreciated, but is now known to be due to concomitant spasm of the arterioles. These patients, although having marked symptoms, do not succumb to the disease, but unless adequate therapy is instituted early, have persistent sequelae which last for years, months, or even for the duration of their lives. In the relatively rare case of superficial thrombophlebitis, there is also pain and fever. Instead of the extremity being white and swollen as it is in the deep thrombophlebitis, there is redness over the involved vein and there is minimal swelling. Superficial thrombophlebitis is usually seen in conjunction with varicosities or is associated with peripheral arterial disease.

Whereas it is our belief that the treatment of phlebothrombosis consists of radical surgery; i.e., ligation of the vein above the site of the thrombus or thrombectomy and ligation after removal of the thrombus, the treatment of thrombophlebitis should be conservative with the exception of the relatively rare case in which there is suppuration.

At the outset it should be emphasized that the treatment of venous thrombosis should consist principally of prophylaxis, and it is our belief that in most instances venous thrombosis can be prevented by the minimization of

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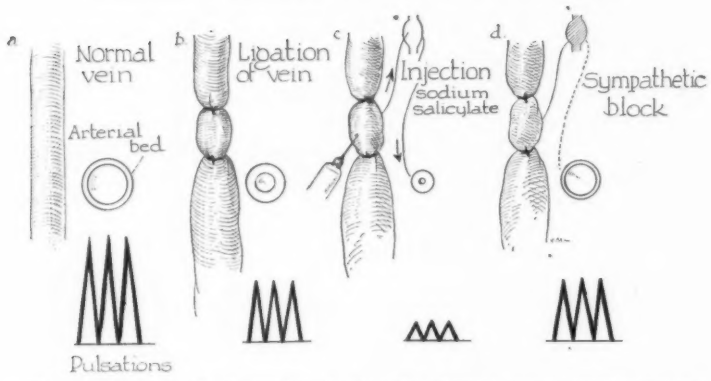

Fig. 1. Diagrammatic illustration showing the effect of experimentally produced thrombophlebitis on arteriolar pulsation. a, The normal findings in the veins, the arteries, and the arterial pulsations as determined plethysmographically. b, The decrease in the size of the arterioles following ligation of the common femoral vein. This results in a decrease in the arteriolar pulsations. c, A marked decrease in the size of the arteriole and a marked diminution in the arteriolar pulsation, following the production of a chemical thrombophlebitis produced by injecting 40 per cent sodium salicylate into the isolated segment of vein. d, The return to normal of the lumen of the arteriole and the arteriolar pulsations, following the blocking of the sympathetic impulses originating in the thrombophlebitic segment. This interruption is produced by anesthetization of the sympathetic ganglion.

trauma and infection, and by the speeding of the circulation in the veins of the lower extremity, venous thrombosis can be greatly minimized. Only after thrombosis has occurred is it necessary that active therapy be instituted. It is a rule on our service that, in all patients past forty years of age who have any tissue injury, operative, accidental, during delivery, or as the result of destruction of tissue by neoplastic disease or infection, the lower extremities are wrapped with compression bandages (Ace No. 8) from the toes to the groin in order to increase the rate of blood flow through the deep venous system. The patient is also made to contract the muscles of the calf and the thigh. Tight abdominal bandages are avoided and the return flow of blood through the venous system to the chest is favored by having the patient take deep breaths. Those positions, such as the Fowler's position, which favor circulatory retardation of the lower extremity are avoided.

Thrombophlebitis of the deep venous system, particularly the femoroiliac, is an interesting biologic phenomenon, because although the lesion is in the large deep veins, the symptoms are the result of arteriolar spasm. Whereas previously it was thought that the pain was due to the inflammatory process in the veins, that the swelling was due to the plugging of the vein by the thrombus, and that the white discoloration was due to the lymphedema, we have been able to demonstrate experimentally and clinically that all of these manifestations are the result of vasospasm. Experimentally, DeBakey, Burch, and I (3) showed that in an isolated thrombophlebitic segment of vein, impulses originate and are carried over the sympathetic nervous system producing spasm of the arterioles of the homolateral extremity (Fig. 1). Subsequently, we (16) showed in clinical cases of phlegmasia alba dolens that there is a very definite diminution in the arteriolar pulsation of the involved extremity, which can be relieved by sympathetic block. (Fig. 2). Concomitant with the relief of the vasospasm, there are relief of pain, prompt subsidence of the fever, and disappearance of the edema. That the edema is not secondary to the mechanical plugging of the vein by the thrombus is demonstrated by the fact that ligating a vein surgically will not produce a similar edema and that the edema in thrombophlebitis will subside quickly following the

chemical section of the sympathetics even though the thrombus still remains. The edema in thrombophlebitis and its persistence are undoubtedly due to the associated vasospasm of the homolateral arterioles, resulting in such a marked diminution in blood flow through the capillary bed that a relative anoxia of the capillary endothelium ensues. Because of this, the permeability of the capillary endothelium is increased and there results an excessive exudation of fluid to the outside, producing the edema. The edematous fluid has difficulty in getting back into the vascular system for two reasons; first, because the pump which is responsible for the movement of the lymph, namely, arteriolar pulsation, is lost because of the arteriolar spasm, and, second because spasm of the venules increases the pressure at the venule end of the capillary and inhibits absorption at this point. By overcoming the vasospasm by anesthetization of the sympathetic ganglia, the pain which is the result of ischemia is relieved and because of the prompt re-establishment of the normal circulation through the capillary bed, the relative anoxia is overcome, the excessive exudation to the tissue spaces is prevented, and, by the re-establishment of the normal arteriolar pulsation, the pump which is responsible for the movement of lymph is again brought into action and the edema quickly diminishes. Prompt subsidence of fever following novocain anesthetization of the lumbar sympathetic ganglia in phlegmasia alba dolens is probably due to the more rapid resolution of the inflammatory process in the vein wall resulting from better vascularization.

Because of the demonstration of these vasospastic phenomena associated with thrombophlebitis and their relief by anesthetization of the regional sympathetic ganglia, the treatment of phlegmasia alba dolens by sympathetic block is rational. Also the fact that these patients who would otherwise be incapacitated for weeks or months with persistent postphlebitic edema, recurrent erysipeloid infections, and recurrent ulcerations are well within a few days' time is additional proof of the adequacy and efficacy of blocking of the sympathetic ganglia in the treatment of phlegmasia alba dolens.

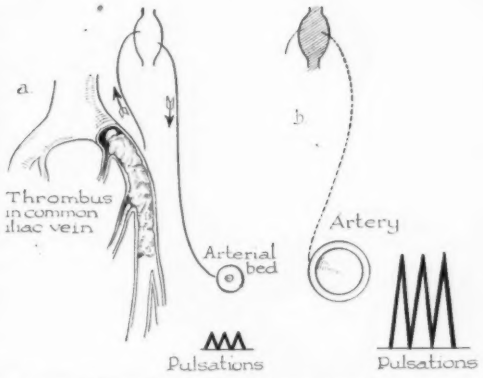

Fig. 2. Diagrammatic illustration of the effect of thrombophlebitis on the arterial bed and on the arterial pulsations. As shown in a, impulses originating in the thrombophlebitic segment, which are carried over the sympathetic nervous system to the arterial bed, produce a marked decrease in the size of the lumen of the vessel and a diminution in pulsation. b, Following anesthetization of the sympathetic ganglia, there is an interruption of these vasoconstrictor impulses, resulting in a return of the arterial lumen to normal and a re-establishment of normal pulsation

The technique of lumbar sympathetic block is extremely simple and has been described adequately in previous reports (13–15; 4, 16–18;) (Fig. 3). Although, theoretically, the employment of a single needle is sufficient, it is our belief that if one uses multiple needles the block is much more likely to be successful, because at best the injection is done blindly. With multiple needles, the chances of striking the level in which the sympathetic chain is located are greatly increased. Because the patient with phlegmasia alba dolens is usually quite ill, we prefer performing the sympathetic block with the patient in the lateral decubitus position. Points two finger breadths lateral to the spinous processes of the first, second, third, and fourth lumbar ganglia are chosen. A cutaneous wheal is made. A long, fine special needle, 5½ inches in length, is used. It is important to use a long needle because otherwise the anesthetic solution may be deposited into psoas muscle. The needle is introduced perpendicular to the skin until the point hits the transverse process. The transverse process serves as a landmark, because, whereas there may be considerable difference in the thicknesses of the subcutaneous fat and the sacrospinalis muscle of a large, muscular,

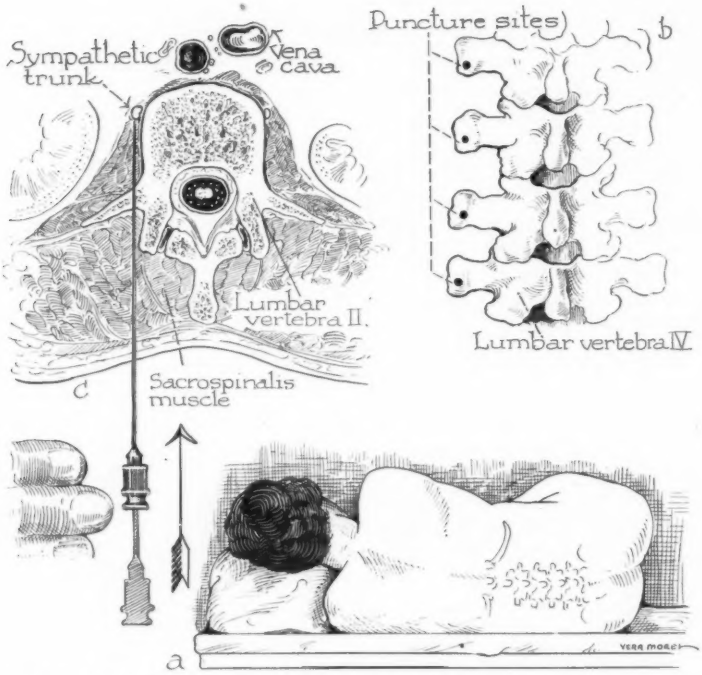

Fig. 3. The technique of lumbar sympathetic block in the treatment of thrombophlebitis. The patient is placed in the lateral decubitus position, because usually these patients are too ill to be placed in a prone position. b, Points are chosen two finger breadths lateral to the spinous processes of the first, second, third, and fourth lumbar vertebrae. Because the spinous process of the lumbar vertebra extends vertically from the body, it represents the level of the transverse process, c. Through the cutaneous wheal, produced at each point two finger breadths lateral to the spinous process, a 5½ inch fine needle is introduced perpendicular to the skin until it impinges against the transverse process. The transverse process serves as a landmark, because whereas the differences in the thicknesses of the subcutaneous fat and sacrospinalis muscle of a large, obese man and a little, thin woman varies considerably, there is relatively little difference in the bodies of their vertebrae. As soon as the needle impinges against the transverse process, its direction is changed slightly either above or below and is introduced for an additional two finger breadths. The point of the needle lies on the anterolateral surface of the body of the vertebra where the sympathetic chain is located. Through each of the four ports, the second, third, and fourth, 5 cubic centimeters of 1 per cent novocain is injected. Immediately following the introduction of the novocain, the patient is placed in the supine position for a minimum of 10 minutes.

obese man and a small, slender woman, there is relatively little difference in the thicknesses of the bodies of their vertebrae. After the transverse process has been impinged with the point of the needle, the direction of the needle is changed slightly, either above or below the transverse process, and the needle is introduced for an additional two-finger breadths. The point of the needle then lies at the anterolateral surface of the body of the vertebra, where the sympathetic chain lies. Through each one of the four needles, 5 cubic centimeters of 1 per cent procaine is injected. The injection is done on the affected side and should be repeated every 24 hours as long as the patient has fever, because the persistence of fever probably is an indication of the persistence of the inflammatory process which is responsible for the vasospasm. Although the pharmacologic effect of procaine lasts only

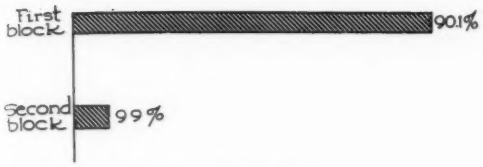

Fig. 4. Relief of pain.

from 1 to 2 hours, we believe that the physiologic effect of the injection of this agent into the sympathetic nervous system is a good deal longer.

In addition to the injection of the sympathetic ganglia, we believe that patients with phlegmasia alba dolens should be treated by active mobilization. Compression bandages, (Ace No. 8) are applied from the toes to the groin, and the patients are made to contract their muscles against a resistance. As soon as the fever has subsided, they get out of bed and walk. They are not allowed to sit in a chair, because we feel that the likelihood of stasis in the veins of the dependent legs when the patient sits is much greater than when the patient lies horizontally in bed and actively contracts his muscles against a resistance.

The results obtained by the use of novocain anesthetization of the lumbar ganglia in cases of typical phlegmasia alba dolens have been very satisfactory. There has been complete and permanent relief of pain in 90 per cent of instances following first block, whereas in 10 per cent of the cases a second block was necessary to give permanent relief (Fig. 4). There is a rapid subsidence of edema. Fifty-six per cent of the cases had a normal extremity within 4 days or less. In 32 per cent the extremity was normal in from 5 to 8 days, in 8 per cent from 9 to 10 days, and in 3 per cent from 11 to 12 days (Fig. 5). Sixty-five per cent of the patients were fever-free within 48 hours after the institution of therapy, 23 per cent in 3 to 5 days, and 7 per cent in 6 to 8 days. In only 4 per cent did the pyrexia last longer than 8 days (Fig. 6). The economic importance of this therapy is exemplified by the fact that 70 per cent of the patients were discharged from the hospital with normal extremities and were fever-free within 4 to 8 days after the institution of therapy; 19 per cent left the hospital between the ninth and twelfth days, and only 11 per cent remained in the hospital after 12 days (Fig. 7). Many others have reported similar results (1, 2, 5, 6–8).

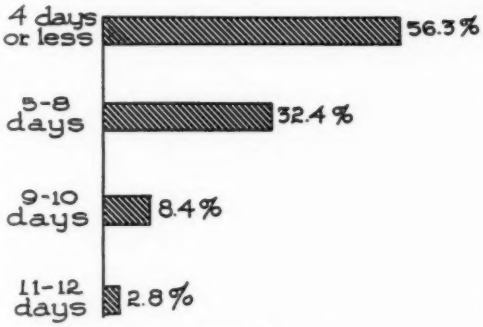

Fig. 5. Relief of edema.

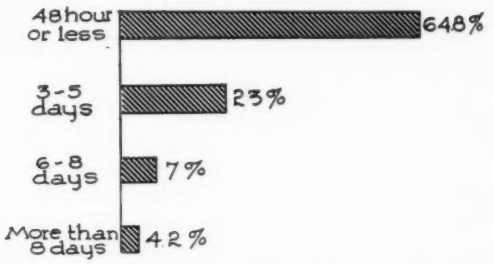

Fig. 6. Subsidence of fever.

Whereas we believe that in all cases of phlebothrombosis and in cases of suppurative thrombophlebitis all patients must have ligation of their veins, we do not believe that venous ligation of the uncomplicated case of phlegmasia alba dolens is necessary, because in such a case the symptoms are due to arteriolar spasm resulting from the inflammatory process in the deep veins, and, although some of these vasospastic impulses are probably interrupted by ligating the vein, this seems an

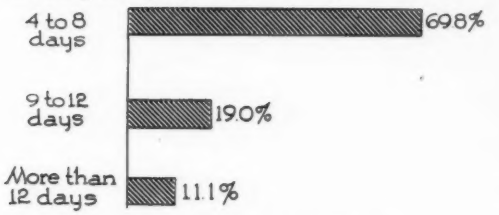

Fig. 7. Duration of hospitalization.

unnecessary procedure when better results can be obtained more safely and more simply by sympathetic block with procaine.

CONCLUSIONS

1. Because the symptoms and signs in true uncomplicated deep vein thrombophlebitis (phlegmasia alba dolens) are due to spasm of the arterioles of the involved extremity, vasodilatation produced by section with procaine of the regional sympathetic ganglia is rational.

2. Although ligation of the involved vein is imperative in phlebothrombosis and in suppurative thrombophlebitis in order to prevent emboli gaining entrance to the systemic circulation, sympathetic block is sufficient in suppurative thrombophlebitis.

3. By the prompt induction of vasodilatation, the symptoms and signs in phlegmasia alba dolens are quickly alleviated and the postphlebitic sequelae are eliminated.

4. The use of multiple needles in performing sympathetic block greatly enhances the efficacy of the injection.

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ANTICOAGULANTS IN VENOUS THROMBOSIS AND THE PREVENTION OF PULMONARY EMBOLISM

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THE object of this paper is to discuss the effect of anticoagulants in the treatment of venous thrombosis, its prevention, and the prevention and treatment of pulmonary embolism.

To approach this problem it seemed logical to consider the subject under the following headings:

1. Whether or not venous thrombosis is infective in origin. It is my impression, as stated in a previous paper (7), that in only 0.5 per cent of the cases of venous thrombosis was infection a factor in production of the thrombus and even in these cases it is possible that the infection was a secondary invasion of a thrombus or clot which had formed from other sources. This evidence is based on the fact that in 28 cases of venous thrombosis which were operated upon, cultures taken from the surrounding tissue, from the wall of the vessel and from its lumen, showed no growth of organisms on ordinary cultures, anaerobic cultures, or on special media. The fact also that in the majority of cases, if the extension of thrombosis can be prevented, they clear up rapidly without further evidence of infection or suppuration, lends further support to this view.

2. The beginning and extension of the thrombus. On clinical evidence, which was supported also by experimental evidence, I think it can be safely assumed that whatever may be the factors precipitating the thrombosis, the lesion begins in a localized area and extends from such area as a propagating thrombus. This is well demonstrated in the cases in which the clinical signs and symptoms would indicate that the calf muscles may be the site of origin. From that point the progression of thrombosis with clinical symptoms and signs extends through the adductor region to involve the femoral and presently the iliac vessels. In many cases at a later period the opposite leg is involved in what would appear to be a retrograde fashion. Also in the post mortem study of the vascular tree of the lungs in patients dying of pulmonary embolism, the primary embolus has been well demonstrated and on top of that has been built up a thrombus which is of more recent duration, which extends more widely through the vascular tree, until ultimately a fatal effect is produced —a fact which has been well demonstrated by Professor Boyd.

3. Ligation of vessels an exciting cause. There is evidence to suggest, both clinically and experimentally, that ligation of vessels, especially veins, may be the exciting cause for thrombosis, from which extension can occur. This is well known in operations involving dissection and removal of organs in the pelvic region where thrombosis with pulmonary embolism as a complication, is a fairly common occurrence. It has been demonstrated experimentally that if any major or minor vessel is divided, tied, sewn or allowed to become occluded by natural clotting and thrombosis, that there is a process of thrombosis set up which extends proximally through that vessel for varying distances. In a vessel very carefully dealt with, these thrombi may be only small fragments occurring in chinks in the vessel where it is gathered into a cone by ligation or where there are small irregularities from suture of the end of the vessel. However, once this process is set in action it is purely a matter of accident just how far it will extend, if the other conditions favoring thrombosis are present. It is suggested, therefore, that any form of surgery on the vascular tree, especially on the venous side, is not without some hazard as regards the initiation of this process of thrombosis with the unpredictable accident of pulmonary embolism as a complication.

From the Department of Surgery, Toronto General Hospital.
Presented in the symposium on Venous Thrombosis and Prevention of Pulmonary Embolism before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–20, 1946.

It would seem obvious, therefore, if thrombosis and clotting can be prevented or is not initiated, that pulmonary embolism cannot occur, leaving out for the moment, of course, fat embolism. Much has been done in the way of clinical care of patients in an attempt to prevent early thrombosis in the vascular tree and from statistics in our own hospital the incidence of thrombosis and pulmonary embolism has been considerably reduced by care of the patient on the operating table and the avoidance of many of the conditions which are condusive to thrombosis. It may be stated emphatically that with the ultimate in view, if by any means, including giving anticoagulants, thrombosis in the venous tree could be prevented, then the solution of pulmonary embolism and the late effects of thrombosis in vessels would be eliminated. It is obvious, of course, that there are difficulties and objections to giving anticoagulants with this objective. For example there are groups of patients in whom the administration of an anticoagulant must be undertaken with great caution. In the postoperative group there may be the danger of initiating hemorrhage into the wound or in the operative field. However, if the surgeon has in mind that an anticoagulant may be used, if the larger or medium sized vessels are adequately dealt with by ligatures, the danger of this is exceedingly small and this danger can be reduced to an absolute minimum by the careful administration of the anticoagulant and its proper control so that the clotting times and prothrombin times are kept within normal and reasonable limits as advocated in the early studies on these subjects. As well there is the added work and difficulty required in such treatment. However, with the proper control and a fine understanding of the objective and the principles, these difficulties are not insuperable and, in my experience, they justify the end-results.

I quite agree, for example, in varicose veins with localized thrombosis in a varix, that ligation with continued activity of the patient, offers simple and adequate relief of symptoms and almost certainly eliminates or prevents complications such as pulmonary embolism or extension to the main vascular tree. On the other hand, with widespread thrombosis through an uncertain area, it is more difficult to know just where ligation would be effective in loculating the area of thrombosis, to prevent further embolism. In my experience the question regarding the terminology of phlebothrombosis versus thrombophlebitis rests on the knowledge of the pathology of the course of events in thrombosis in the venous tree. As every operator has demonstrated, there may be thrombosis of vessels far in advance of the area suggested by clinical symptoms or physical findings of edema, tenderness, etc. As was explained in an earlier paper, I believe these effects are, as stated by Dr. Homans many years ago, the result of the inflammatory reaction to a thrombus which has formed some hours or days previously. These inflammatory changes provide the patient with the cause of his symptoms, and the surgeon, with the findings of thrombosis. It is obvious, therefore, that the extent of the thrombus in the vascular tree is exceedingly difficult to delineate by physical examination. Also phlebography has given only partial satisfaction in delineating the uppermost extension of such a thrombus. As the surgeon has the objective, in tying vessels, of loculating the process below his ligature, difficulties immediately arise. It is just here that anticoagulants enter into their best atmosphere. The effect throughout the vascular tree is universal and thrombosis, no matter where it is or where its extensions may proceed, comes under the influence of anticoagulants. This is just as true in the question of further extension of thrombosis when embolism has occurred in the pulmonary artery, as well as in the distal tree. It also has the advantages of having its effect in preventing intracardiac thrombosis (5). Especially is it true in the prevention of thrombosis in surgery either on the arteries (6) or on the veins themselves. I have found it of very great value in doing anastomoses as first done by Blalock, and have used it in 15 cases of the Tetralogy of Fallot. In none of these patients has there been thrombosis at the site of anastomosis as far as one can determine clinically and in none has there been cerebral thrombosis or other cerebral accidents; neither has there been any evidence of pulmonary or peripheral embolism.

My evidence as regards the effect of anticoagulants on venous thrombosis and pulmonary embolism, is based on:

1. Four hundred postoperative cases in which patients were treated with an anticoagulant with the objective of cutting down the incidence of thrombosis and consequently of pulmonary embolism. In this group no patient developed peripheral thrombosis and there were no cases of pulmonary embolism. Our experiment obviously includes too few cases to be of much significance except that the treatment was carried out in groups of cases in which, from our hospital statistics, thrombosis and pulmonary embolism reached the highest figures recorded.

2. Three hundred and seventy-one cases of venous thrombosis, in which treatment by anticoagulants was carried out with the objective of (a) preventing pulmonary embolism and (b) as treatment for the progressive thrombosis in the venous tree with a hope of relieving symptoms and of diminishing the ill effects so obvious and evident following venous thrombosis, such as persistent edema, varicose veins, ulceration, etc. All these patients had typical symptoms and signs of venous thrombosis before treatment was started.

The results of treatment were satisfactory in that none of the patients had pulmonary embolism. Moreover, the late effects of the thrombosis were less severe than in a control group. There was less persisting edema, fewer ulcers in a 9 year period and fewer varicose veins during this time.

3. One hundred and forty-nine cases of pulmonary embolism treated by anticoagulants. The cases were not selected and were obviously those which had survived the first embolism. In many of these the patients were *in extremis* at the time of beginning of treatment. Fifty-two of these presented a state with which you are all familiar: the patient in alarming shock, with no palpable pulse at the wrist, bordering on unconsciousness and with all the serious and dreadful effects of massive pulmonary embolism. From an analysis of histories of the hospital, together with the postmortem findings, it has been demonstrated as shown on a previous paper, that about 1 in 5 of all cases surviving the first pulmonary embolism is apt to succumb to future embolisms or from the effect of propagating thrombosis increasing the effect of the original or subsequent emboli.

This group of patients with pulmonary embolisms here reported are those over whom I had control during treatment. In these I had information that the treatment was adequate, that the necessary effect on the clotting time or on the prothrombin time was obtained. I saw a fairly large number of similar cases in consultation with other doctors who undertook the treatment of the patients and for that reason these are not included in this report. I have learned subsequently of 3 deaths in this group treated by other doctors. In those in whom I had control of the treatment and knew that the adequate effects on the clotting and prothrombin times had been obtained, there were no deaths from embolism in 149 cases. Four of these, following the beginning of treatment, had further embolisms which were obviously small in nature because they produced only slight effects on the patient.

It is very impressive to see the effect on a patient with massive pulmonary embolism or with extensive thrombophlebitis or both; the improvement that takes place in a matter of very few hours is striking, once the effect on clotting time has been obtained. The pulmonary distress with dyspnea, pain, etc. together with the embarrassment of heart action are diminished progressively in relatively short time so that within a few hours there is a measurable change and within 24 to 36 hours the alarming symptoms have largely disappeared. It may take several more days before there is complete relief of all symptoms.

During the course of such treatment, it has frequently been observed that there was no obvious swelling or edema of extremities at the time of the massive embolism. However, during the course of treatment one leg has enlarged and showed "quite marked edema and on some occasions, at the same time, or within a few days the other leg has gone through similar changes. It is my impression from a study of the pathology that this is no indication of ineffectiveness of the treatment by anticoagulants. I believe that at the time of the embolism there obviously was a massive thrombus at some site in the venous tree

which was so insecurely attached that it broke off and floated as an embolus. However, at this stage the inflammatory reaction in the wall of the vein and surrounding tissue had not reached the point where it had produced clinical symptoms. Even under the treatment by the anticoagulant, which can only prevent the further extension of thrombosis, the remaining thrombi have excited the inflammatory reaction which has gone through the changes necessary to healing of the lesion.

To accomplish this effect, in the presence of thrombosis or embolism, it is absolutely essential that the original principles of application of anticoagulants be followed. First, if heparin is administered, it must be carried to the point where the clotting time in the patient is kept at or about 15 minutes. It is of no use whatever to give heparin blindly and not know that the effect is being obtained. Because the effect of heparin is so evanescent, and because the dose is variable for the individual, the only safe way to be sure of this effect, is to do clotting times at short intervals. The next principle is to give the anticoagulant until the healing process in the area of existing thrombosis has reached the stage where no further thrombosis will take place. From our experience, in the average patient who is able to get out of bed, the patient is kept at rest for 3 or 4 days under the treatment. Following this, exercise is encouraged and within 6 or 7 days of the beginning of treatment, the patient is urged to be out of bed and exercising actively. When the patient can go through this with some energy, probably on the seventh, eighth, or ninth day, the heparin treatment is discontinued. If, however, the patient has some lesion or operation which necessitates staying in bed, then the treatment is continued for longer periods up to 3 and occasionally 4 weeks, in such cases as spinal fusion where the patient has not been allowed to be out of bed. It was demonstrated experimentally that a thrombus placed in a vessel is endothelialized well within this period of time, and probably that is the best protection against further extension, provided the remaining physiology of the patient has reached normal.

Dicoumarol has many advantages over heparin in the way of expense and the ease of administration. However, in my experience it is not quite as effective as is heparin, in preventing extension of thrombosis. It can be used, however, as an important adjuvant. When the patient has begun treatment with heparin for 2 or 3 days, the dicoumarol can be added as a supplement and the patient encouraged to be ambulatory under this treatment with greater ease.

I have not used any of the thrombolytic substances in an attempt to dissolve clots. A few patients were treated with sodium tetrathionate, but not enough to determine its value. In those treated, the effect seemed to be excellent.

Dr. Allen at the Mayo clinic has reported (1) a large group in which anticoagulants were administered with excellent effects. Also, the group in Scandinavia, namely Zilliacus, Hedenius, Jorpes have reported large groups treated with anticoagulants with satisfaction.

One advantage of using anticoagulants also is that in a patient who is on the verge of collapse, the treatment involves very little disturbance and in my experience the effect has been dramatic. This may have advantages over operative procedures where either injection or operation involves the undertaking of more active and energetic measures for which a patient may be in very poor condition.

CONCLUSIONS

1. Intravascular thrombosis and clotting can be prevented by anticoagulants, heparin, and dicoumarol.

2. If thrombosis and clotting have occurred, anticoagulants in appropriate doses will prevent further extension of the process.

3. If a patient is adequately treated with anticoagulants following pulmonary embolism, the chances of survival are excellent.

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CARCINOMA OF THE COLON

A Statistical Analysis

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THIS paper represents a study of all the patients with carcinoma of the colon, not including the rectum and rectosigmoid, admitted to the Veterans Administration Hospital, Hines, Illinois, from 1931 to 1945 inclusive. A similar review is being made by other workers at this Hospital on carcinoma of the rectum and rectosigmoid. During this 15 year period, this institution has been the tumor center for all Veterans hospitals of the Midwest, and a large volume of material and records is available for study and analysis.

The purpose of this paper is to add to the growing number of cases being reported so that totals of statistical significance may be amassed, to analyze the material, and to attempt to draw pertinent conclusions. Each record of admission was studied with reference to age, duration of symptoms, common complaints, important physical and laboratory findings, surgery, operative mortality, effects of irradiation, pathology, and numbers and length of survivals. It is a difficult task to take a maze of data and present conclusions in a simple readable form. Follow-up records are practically one hundred per cent complete because of government pension regulations and the persistent efforts of a specially created tumor registry section.

There were 131,279 admissions of all types during this 15 year period, and 16,097 (primary admissions) of these were patients with carcinoma. In 1330 of these admissions, the primary lesions were in the large bowel, colon, and rectum included. In Figure 1 are shown the sites of predilection. Many writers have repeatedly stressed that two-thirds of all carcinomas of the large bowel involve the rectum and rectosigmoid and can be felt by the finger of the careful examiner. These and certain others in the lower sigmoid likely to be missed by barium enema can be seen through the proctosigmoidoscope, and specimens obtained for biopsy study. Points of flexure and the cecum have a moderately high incidence considering their short span. They presumably receive the maximum mechanical and chemical trauma which might play a rôle in carcinoma of the colon.

The close similarity in the frequency of the sites of involvement in our patients with those reported by others is shown in Table I, and is of biological significance.

This study concerns itself primarily with the 486 patients who had involvement above the rectosigmoid. The histories were divided into two groups, before and after January 1, 1941. This division is convenient because it gives data as to 5 year cures and because of the adoption of improved methods in anesthesia and in preoperative and postoperative care in the latter period. These included better colon decompression, the various sulfa drugs, later penicillin, and liberal use of blood transfusions and continuous gastric suction. Their salubrious effect on surgical mortality and morbidity seems clinically and statistically to have ushered in a new era in colon surgery.

In Figure 2 are given percentages of resectability for the entire period. In the term resectable are included only those cases in which a cure can reasonably be anticipated following removal of all gross carcinomatous tissue. It includes those in which adjacent resectable organs and lymph glands are involved. A nonresectable lesion implies distant metastatic spread to liver, lung, bone, brain, or nonremovable lymph glands. In the nonresecta-

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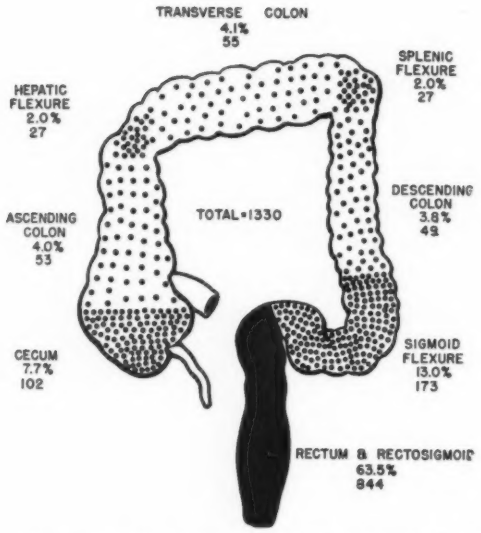

Fig. 1. The sites of involvement of carcinoma of the colon and rectum.

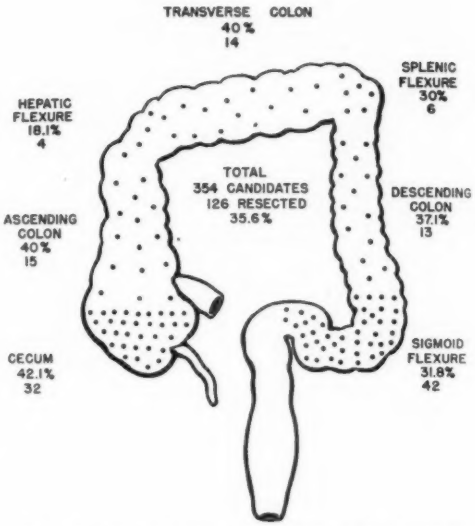

Fig. 2. The percentage of patients with resectable (curative) carcinoma of the colon.

ble group, resection when possible by primary anastomosis has been done and does add to the comfort and longevity of the patient. However, such cases are not included as resectable for possible cure.

The percentage of resectables is lower at Hines Hospital than at many other hospitals, but it must be pointed out that numerous cases of veterans with this affliction still in a favorable stage for surgery have been operated upon successfully elsewhere and have never reached Hines. A large proportion of unfavorable cases have been sent here for "palliative irradiation" and terminal care. In determining resectability percentages at Hines, all patients who had undergone surgery elsewhere, either with successful resections or hopeless explorations, were excluded. All other patients, regardless of the extent of the disease, are included in the total regarded as candidates for possible resection. Also included are patients explored elsewhere and in whom there was doubt as to resectability. Subsequent exploration at Hines in numerous instances revealed resection to be actually possible with gratifying results. This was frequently true when there was a complicating abscess magnifying the pathology at the original exploration. However, it is obvious that at an institution such as this, open to all veterans, many hopeless cases must necessarily gravitate. Thus, though the percentage of resectables in the entire group is expected to be low, the failure to improve appreciably the number in the resectable group in the

TABLE I.—A COMPARISON OF THE ANATOMIC DISTRIBUTION OF CARCINOMA OF THE LARGE INTESTINE IN PATIENTS OF THREE TUMOR CLINICS

	Hines Veterans Hospital 1931–1945		Lahey Clinic 1936–1944		Mayo Clinic 1907–1928
No. of cases	1330		1457		3542
Involved sites and percentages					
Cecum	7.7%		6.52%		5.95%
Ascending colon	4		3.30		
Hepatic flexure	2		2.94		
Transverse colon	4.1	15.9%	4.51	17.1%	16.99%
Splenic flexure	2		2.40		
Descending colon	3.8		3.97		
Sigmoid	13.0		12.42%		13.55%
Rectosigmoid and rectum	63.5		62.79%		62.84%

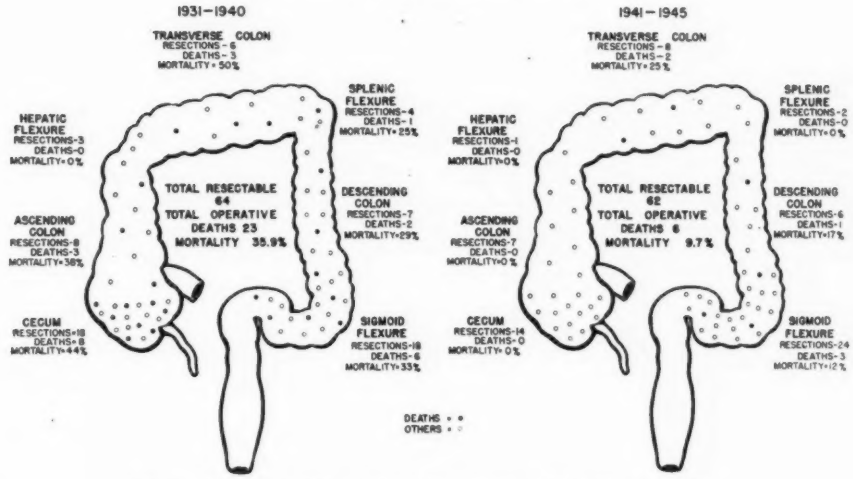

Fig. 3. Mortality within 30 days after resection of carcinoma of colon.

second period is disappointing. There were 33.16 per cent resectables in the 1931–1940 group, and 38.13 per cent in the 1941–1945 group. Actually 48.44 per cent were resected in the latter group but this included 16 "non-resectables" having distant inoperable metastases who were resected with primary anastomosis. The only improvement in resectability in the two periods was observed in the sigmoid group where 23.4 per cent (18 of 77) were resectable in the 1931–1940 group and 43.6 per cent (24 of 55) in the 1941–1945 group. Fortunately most other clinics have reported gratifying increases in the percentage of resectables in recent years. Pack and Livingston state that 70 per cent can be submitted for resection. The Lahey Clinic's 85 per cent resectability rate sets a high mark and will be difficult to exceed until earlier diagnoses are made.

In Figure 3 the operative mortality following resection is shown. Any patient who died within 30 days of operation was arbitrarily included in this group though the majority died in 1 to 10 days. The drop from 35.9 per cent to 9.7 per cent in the "sulfa era" is most encouraging, although just how much importance for this improvement is due to the sulfa drugs remains to be seen. Coller and others have deliberately refrained from using sulfa drugs and have obtained similar drops in mortality rates. Our impression in studying the records of these deaths in the early period was that much of the mortality was due to the erroneous tendency to diagnose complete obstruction, which is very uncommon, operate immediately, and then do too much in an acute obstruction of marked degree.

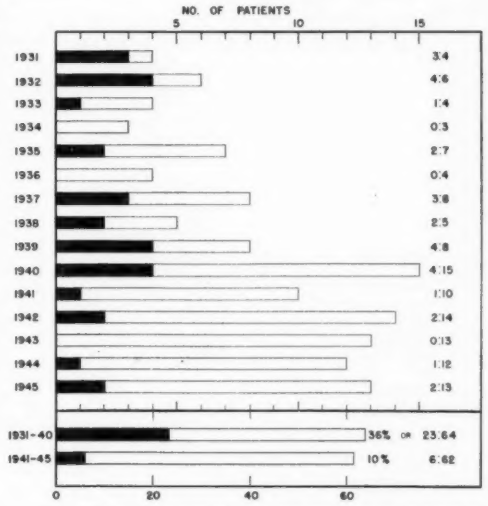

Fig. 4. Operative mortality after curative resections of the colon, by years.

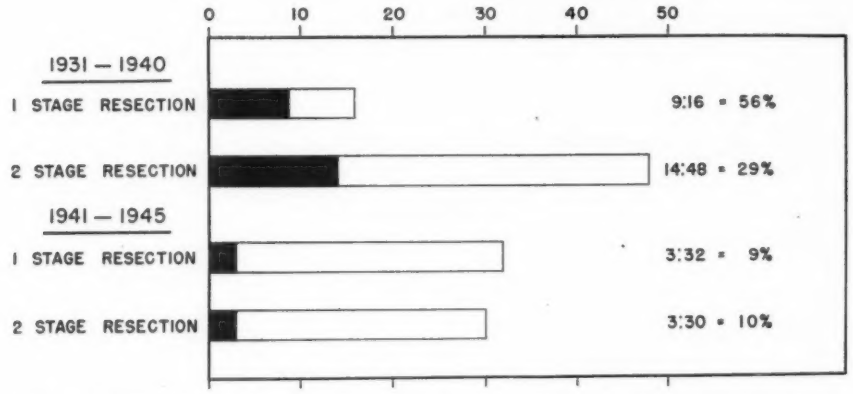

Fig. 5. Number of one and multistaged resections of carcinoma of colon and operative mortality.

Resections in all segments of the colon reflects this statistically significant lowering of the operating mortality but the right half of the colon is especially favored. Pack and Livingston state that an operative mortality of 10 to 15 per cent can be expected if there is no selection of cases. However, with some clinics reporting a surgical mortality of less than 4 per cent, there is ample room for improvement in our results.

Figure 4 shows the operative mortality by years. The change began gradually during 1940 and is striking thereafter. It cannot be attributed to improvement of surgical technique.

In Figure 5 it is noted that resections were done in one stage in only 25 per cent of the 1931–1940 cases, but in 51.6 per cent in the 1941–1945 group. Although the mortality in single and multiple stage procedures in the 1941–1945 group is about the same, the increased number of one stage procedures possible is of great significance since it reduced the period of hospitalization from 2 months or more to 3 weeks or less, and it added to the comfort of the patient. With the present day shortage of hospital beds, the successful shift to one stage procedures is of tremendous value, and is in line with the general trend throughout the nation. The good reason for the early tendency toward multiple stage procedures in the 1931–1940 period is indicated by the mortality rate of 56.2 per cent for the one stage, contrasted with 29.1 per cent for the other.

In Figure 6 the survivals of 5 to 15 years following resections in the 1931–1940 group are shown. Of the 281 colon cases admitted in this first period, omitting those resected or explored elsewhere and sent here for routine x-ray therapy or terminal care, 193 candidates were left for possible resection. In 64 resection was accomplished, and 21 or 32.8 per cent of the resectables are alive today. Of the resectables who survived the operation in that first period when the mortality rate was so high, 51.2 per cent are alive over 5 years. With the lowered mortality rate of the second period, it is to be expected that approximately 50 per cent of the resectables can be offered a 5 year cure, and this is the approximate figure of the most successful tumor clinics. Postoperative prognosis is best in right side lesions.

In 41 cases resection was done elsewhere in the 1931–40 group and the patients were sent to Hines for routine x-ray therapy or terminal care. Of these, 13, or 32 per cent, were alive 5 to 15 years later. Improvement in the surgical mortality rate is gradually reaching a point where for further progress the only means of obtaining more cures is to make earlier diagnoses to increase the percentage of resectables. Herein lies considerable room for improvement.

Figure 7 presents a comparison of the survival of patients following curative resection

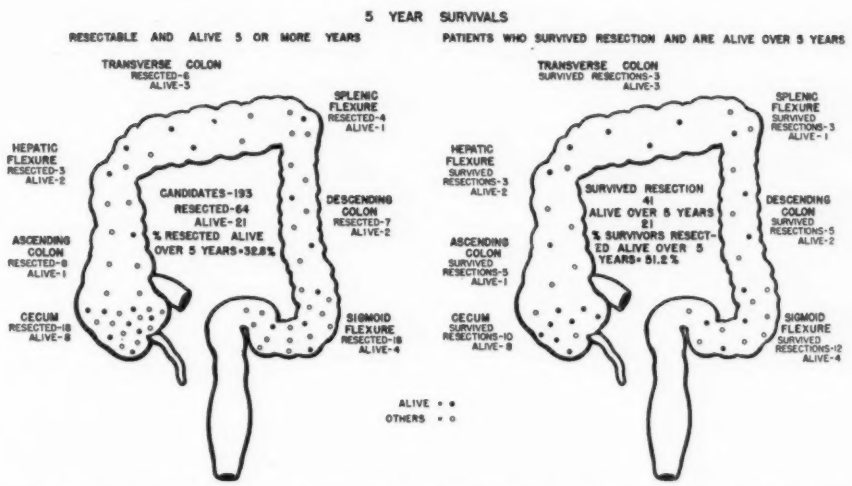
5 YEAR SURVIVALS
RESECTABLE AND ALIVE 5 OR MORE YEARS
PATIENTS WHO SURVIVED RESECTION AND ARE ALIVE OVER 5 YEARS
TRANSVERSE COLON RESECTED-6 ALIVE-3
SPLENIC FLEXURE RESECTED-4 ALIVE-1
HEPATIC FLEXURE RESECTED-3 ALIVE-2
CANDIDATES-193 RESECTED-64 ALIVE-21 % RESECTED ALIVE OVER 5 YEARS-32.8%
DESCENDING COLON RESECTED-7 ALIVE-2
ASCENDING COLON RESECTED-8 ALIVE-1
CECUM RESECTED-18 ALIVE-8
SIGMOID FLEXURE RESECTED-18 ALIVE-4
TRANSVERSE COLON SURVIVED RESECTIONS-3 ALIVE-3
SPLENIC FLEXURE SURVIVED RESECTIONS-3 ALIVE-1
HEPATIC FLEXURE SURVIVED RESECTIONS-3 ALIVE-2
SURVIVED RESECTION 41 ALIVE OVER 5 YEARS 21 % SURVIVORS RESECTED ALIVE OVER 5 YEARS-51.2%
DESCENDING COLON SURVIVED RESECTIONS-5 ALIVE-2
ASCENDING COLON SURVIVED RESECTIONS-5 ALIVE-1
CECUM SURVIVED RESECTIONS-10 ALIVE-8
SIGMOID FLEXURE SURVIVED RESECTIONS-12 ALIVE-4
ALIVE
OTHERS

Fig. 6. Number and percentage of patients surviving 5 or more years after curative resections of the colon, 1931–1940.

for carcinoma of the colon in 1931 to 1940 and in 1941 to 1945. The method of construction of the graph is shown in Table II.

During 1931 to 1940, there were 64 patients with resections. Of these, 64 per cent survived 1 month after the operation, 44 per cent, 3 years, and 39 per cent 5 years. To compare the survival of the patients operated on during 1941 to 1945, it is necessary to analyze the data by years, as shown in the table. In 1941, 10 patients were resected. Of these men 9 survived 1 month and 7 men survived 4 years. As the cases were analyzed early in 1946, the 1941 patients were followed only 4 years, the 1942 cases 3 years, and for the 1945 patients only the 1 month follow up can be used. The results obtained on the 1941 to 1945 patients can be totaled as shown in the table and the percentage of survivors calculated for the entire 1941–1945 group. By this method it is possible to obtain survival curves for the patients that have been operated on within the last five years.

It is seen from Figure 7 and Table II that there has been considerable improvement in the survival of patients after operation. A large part, if not all, of this improvement is evidently due to the fact that a greater percentage of patients died postoperatively in 1931 to 1940 than in later years. To determine whether the improvement in survival is due exclusively to the decrease in postoperative deaths, it was necessary to construct Figure 8 which shows the follow-up of patients who survived 1 month or more after resection. Even after the postoperative deaths are excluded, there is still a higher percentage of survivals in the patients operated on in 1941 to 1945. This suggests that surgeons in recent years were capable of removing completely the

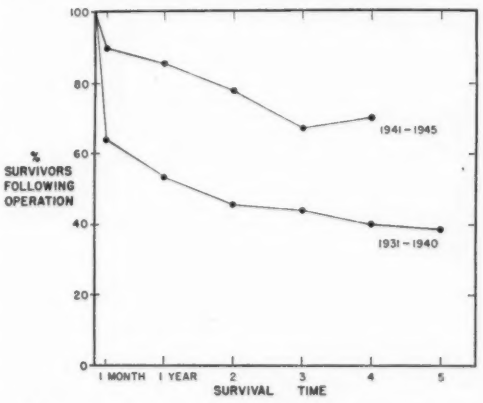

Fig. 7. Survival curves of patients with curative resections for carcinoma of the colon.

TABLE II.—DATA FOR THE CONSTRUCTION OF 1931–1940 AND 1941–1945 SURVIVAL CURES

	No. of patients with curative resections	1 month		1 year		2 year		3 year		4 year		5 year	
		No. survived	No. followed	No. survived	No. followed	No. survived	No. followed	No. survived	No. followed	No. survived	No. followed	No. survived	No. followed
1931–1940	64	41	64	34	64	29	64	28	64	26	64	25	64
Per cent survivors	100	64.0		53.1		45.3		43.8		40.6		39.1	
1941	10	9	10	8	10	8	10	7	10	7	10		
1942	14	12	14	10	14	9	14	9	14				
1943	13	13	13	13	13	12	13						
1944	12	11	12	11	12								
1945	13	11	13										
1941–1945	62	56	62	42	49	29	37	16	24	7	10		
Per cent survivors	100	90.3		85.7		78.4		66.7		70			

tumor in a higher percentage of cases than formerly.

SYMPTOMS

These patients were all veterans, the majority from World War I. They were all males, the youngest was 21, the oldest 77, and in most cases the carcinomas occurred between the ages of 45 and 50 years. Symptoms were present from sudden onset to several years before a diagnosis was made. An average of 6 to 10 months passed between the onset of symptoms and hospitalization. In those found resectable the average duration was 6.3 months, in the nonresectable group 9.7 months. Lahey states that at that clinic the interval for all cases has been 9 months with no appreciable improvement in recent years.

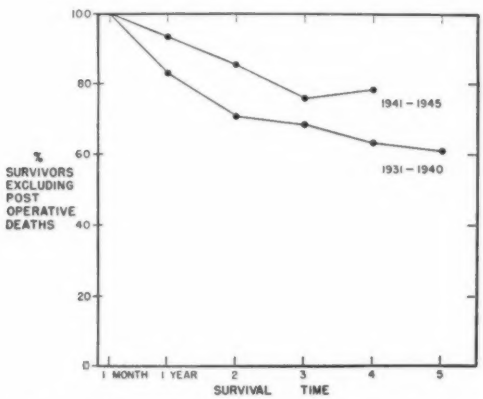

Fig. 8. Survival curves of patients surviving one month or more after curative resections for carcinoma of the colon.

There are no pathognomic symptoms of cancer of the large bowel, but sufficient warning is given to justify study which will usually lead to an accurate diagnosis. Unfortunately, many patients still undergo trial medical treatment, hemorrhoidectomies, or appendectomies before diagnostic studies are instituted. The most common and suspicious complaints are enumerated as follows (Fig. 9):

1. Abdominal distress, frequently more marked in the region involved, though often enough to cause confusion, obstruction of the left colon, may cause most distress in the dilated right bowel. The character of the distress varies and seems to be directly related to the degree of obstruction. It may be dull, but as the lesion tends to be located more toward the left with its semisolid stool and a tendency toward the formation of annular constricting lesions, obstructive pain occurs with colics, nausea, and vomiting. Discomfort is usually aggravated by eating and relieved by bowel movements, especially if the stools are kept liquefied by cathartics. In 7 per cent of left colon lesions an acute obstruction ushered in the first sign of trouble. Fourteen per cent of splenic flexure lesions began in this manner. Gordon Heyd states that 5 per cent of sigmoid tumors begin with acute obstruction. Carcinoma of the cecum is frequently diagnosed clinically as an appendicitis, and appendectomies had been performed on 19 of the cecal cases just before admission to this hospital. Usually the surgeon recognized that there was cecal pathology present at operation.

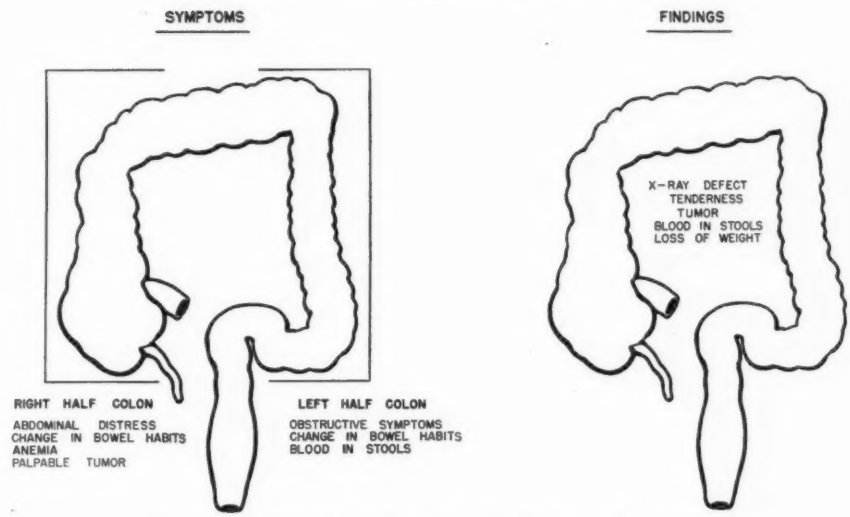

Fig. 9. Symptoms and signs in patients with carcinoma of the colon.

2. *Change in bowel habits* is an important and frequent symptom elicited only by a carefully taken history. Constipation is common regardless of the location of the lesion, but more pronounced and annoying in left half colon pathology. It frequently alternates with diarrhea, often because the patient doses himself with cathartics at regular intervals. However, diarrhea instead of constipation may be the patient's complaint.

3. *Mass in the abdomen* was mentioned by the patient himself in 25 per cent of the cases with involvement of the cecum or ascending colon, 6 per cent of the sigmoid group, and rarely by others. Gordon Heyd states that 10 per cent of the people with carcinoma of the cecum discover a lump in the right side before consulting a physician.

4. *Weight loss*, contrary to the usual belief, is often an early sign and is present in practically all. It may occur rapidly, but ordinarily appears slowly. From 16 to 75 pounds loss of weight was common, but in some patients with a violent obstructive onset there had been no previous loss.

5. *Blood in the stools* is mentioned in the histories of 33 per cent of patients with lesions in the left half of the bowel with their tendency toward the appearance of conspicuous red blood, but only 8 per cent of those with right colon involvement mentioned melena. Unfortunately, the record often fails to note any questioning on this important point.

6. *Other complaints.* Anemia, of an intense degree is always stressed in the literature in connection with cancer of the cecum. It is spectacular and impressive when it occurs, but was uncommon in this series. The red count was usually normal even in the cecal cases until late in the disease when curative surgery was impossible. Only 13 of the 102 cecal cases had a red blood count below 3,000,000. In only 2 patients anemia and weakness were the main complaints. Of the 53 ascending colon lesions, 6 had a red blood count below 3,000,000.

Indigestion, weakness, nausea, vomiting, anorexia and fever were frequently mentioned.

FINDINGS

1. *A palpable mass* was noted at the initial examination by the Veterans' Hospital physician in 81 of the 102 cecal cases, 14 of the 53 ascending colons, 20 of the 27 hepatic flexures, 26 of the 55 transverse colons, 11 of the 27 splenic flexures, 22 of the 49 descending colons, 87 of the 173 sigmoids, averaging 69 per cent.

This is a rather high figure compared to that of others who mention 10 per cent to 33⅓ per cent as having palpable masses on the right, seldom on the left, and again indicates that many of our patients arrive late. However, the palpation of a tumor does not necessarily indicate a hopeless process.

2. *Tenderness* of varying degree is frequently present at the site of involvement.

3. *Occult blood* in the stool was surprisingly seldom searched for, but usually positive if the tests were ordered.

4. *Barium enema x-ray studies* practically always revealed a suspicion-arousing defect which was usually properly interpreted. The segment where pathology was most often overlooked was the sigmoid in which x-ray studies missed the lesion in 9 per cent of these cases.

5. *Proctoscopy* following digital rectal examination is without a peer in lesions up to 23 centimeters from the anus.

PATHOLOGY

Pathology was proved by microscopic studies in 68 per cent of the series. Autopsies were secured in 145 (37%) of the 390 known dead.

Adenocarcinoma or a colloid modification was the usual finding, occasionally an undifferentiated carcinoma. In lesions thought by the operator to be nonresectable, a large, firm mesenteric gland was frequently taken for biopsy, and the pathologist's report was usually negative for carcinoma. This implies that neither surgeon nor pathologist is able to diagnose cancer of the lymph nodes grossly or to differentiate from inflammation. A frozen section at operation might prevent classifying a condition as inoperable.

Operative deaths were usually due to peritonitis, embolism, pneumonia, shock, and myocardial damage. One cecal case succumbed to gangrene of the terminal small bowel after resection due to thrombosis of the ileocolic artery.

Multiple polyposis was noted by the pathologist, surgeon, proctologist or roentgenologist in 11 (2.2%) of the 486 patients of this study. The primary carcinoma in these cases was located as follows: cecum, 2; transverse colon, 3; splenic flexure, 1 (this patient also had a concommitant cancer of the hepatic flexure); descending colon, 4; and sigmoid, 1.

In 3 instances in this entire series multiple cancers of the large bowel were found. Perforations into small bowel and stomach were noted in a few instances. Bladder attachment, but not perforation, was occasionally mentioned. Hydronephrosis secondary to carcinomatous obstruction of the ureter seldom occurred. Abscesses often complicated the picture, and required preliminary drainage.

IRRADIATION

Irradiation was used frequently as a "palliative" measure in the earlier years with no outstanding improvements. Doses of a total of 100 to 6,000 roentgens are reported, but deep therapy is no longer considered of much value for lesions above the rectosigmoid. It was felt that x-ray therapy following drainage of abscesses definitely shortened the period of waiting preparatory to radical surgery.

AVERAGE SPAN OF LIFE

In the inoperable cases death occurred 11 months after onset of symptoms, a speed which suggests a vicious process. In those having a simple exploration, death occurred 6 months after operation and 16 months after onset of symptoms. Those who underwent palliative resections lived 17 months after operation. As had been shown previously, the majority who died after attempted curative resections did so in the first and second years but some died of recurrence as late as 6 years following operation.

SUMMARY

A survey has been made of the 486 cases of carcinoma of the colon seen at Hines Veterans Hospital, Hines, Illinois, during the past 15 years. The sites of predilection are almost identical with large groups reported elsewhere. The resectability rate of 35.6 per cent is low. The drop in the mortality rate following surgery from 35.9 to 9.7 per cent in recent years is encouraging. The 5 year survival rate approaches the 50 per cent figure of the larger clinics. More one stage procedures are being done in recent years. A review of pertinent data is given.

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ANTICOAGULANT THERAPY IN THROMBOSIS

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THE specific treatment of thrombosis seems to demand the use of anticoagulants. Thrombosis arises through intravascular clotting of the blood; a pulmonary embolism is simply a fibrin clot detached from the walls of a peripheral vessel. In the past considerable attention has been paid by such men as Morawitz, Howell, and others, to the possibility of using anticoagulants to prevent thrombosis. Although heparin, the natural anticoagulant of the body itself, was discovered in 1916 by MacLean,[1] working with Howell, very little benefit came of it during the next 20 years. As early as 1933 Charles and Scott of Toronto elaborated a method for large scale extraction of heparin from liver and lungs and the chemical nature of the drug was elucidated 2 years later (Jorpes). Thanks to these efforts heparin has been made available. Crafoord of Sweden and Murray of Toronto were the two surgeons first to use heparin clinically.

PROPHYLACTIC USE OF HEPARIN

During the years 1935 to 1940, it was clearly demonstrated that postoperative thrombosis and pulmonary embolism could be prevented if heparin were administered in adequate doses over an adequate length of time. In Sweden, Crafoord, Wetterdal, and Leissner heparinized about 800 patients postoperatively and in Canada Murray reported the results in treating 400 patients in the same way. Although a high incidence of thrombosis was expected, 2 or even 4 per cent, practically no complications occurred. Two hundred fifty milligrams of heparin a day was found to be an adequate dosage. In the Swedish series heparin was given to 657 patients, the treatment being started on the second or third day after operation or childbirth.

Similar successful results have been reported from the use of dicoumarol. Barker and his co-workers at the Mayo Clinic administered dicoumarol postoperatively to 1,000 patients and in Sweden, Bruzelius treated 1,600 patients in the same way. In each series there was a marked decrease in the number of thrombotic complications.

Because of the expense involved and the risk of hemorrhage there will, however, be no question about giving heparin or dicoumarol to every patient after operations or childbirth.

Prophylactic treatment with anticoagulants must be restricted to cases in which the risk of a thrombosis occurring is considerable, e.g., after parturition in a patient who has had thrombosis during pregnancy, or after operations on patients who have suffered from earlier repeated thromboembolic attacks after operation, childbirth, or miscarriage. In such instances heparin has frequently been used in Swedish hospitals, starting with 50+50+50 +100 milligrams of heparin a day at 8, 12, 16, and 20 hours, from the second or third day onward for 5 to 8 days, until the patient is able to get up and can move about freely.

Presented in the symposium on Venous Thrombosis and Prevention of Pulmonary Embolism before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–20, 1946.

[1]For references see Jorpes, E. Heparin in the Treatment of Thrombosis. 2d. ed. New York and London: Oxford University Press, 1946.

TABLE I.—HEPARIN TREATMENT OF THROMBOSIS AND PULMONARY EMBOLISM AT THE MARIESTAD HOSPITAL, SWEDEN, 1940–1946

	No treatment 1929–1938	Heparin treatment Oct. 1, '40–Sept. 30, '46
Number of patients admitted	25,628	20,002
Number of thrombosis cases	264	258*
Fatal embolism	47	3
Mortality among thrombosis cases	18%	1.1%
Average duration of stay in bed	40 days	4.6 days
Disabling after-effects	Serious	None or very slight

*104 patients were admitted to the Mariestad Hospital because of thrombosis.

TABLE II.—RESULTS IN A SERIES OF THROMBOTIC CASES TREATED WITH ANTICOAGULANTS, MAINLY HEPARIN, DURING 1940–44

	Without anticoagulants		With anticoagulants	
	Cases	Deaths	Cases	Deaths
Medical Clinic A	16	9	22	0
Surgical Clinic A	71	17		
Surgical Clinic B	41	5	26	0
Surgical Clinic C			74	0
Surgical Clinic D	33	11	31	1
	161	42	153	1

The Surgical Clinic C is that of Dr. Crafoord.

The anticoagulant therapy was combined with exercises and early ambulation.

THERAPEUTIC USE OF HEPARIN

Anticoagulant therapy has been found fully effective in the treatment of thrombosis. Even in his first reports on the use of heparin, Murray, in 1938, reported on 35 cases of spontaneous thrombophlebitis and pulmonary embolism and in 1939 on 72 cases treated with heparin, and the results were very good.

In Sweden, Gunnar Bauer at Mariestad Hospital found that incipient initial thrombosis in the legs, as shown by phlebographic x-ray examinations, was checked by heparin treatment; heparin aborted early thrombosis. The acute symptoms, the pyrexia, swelling, tenderness, and pain in the legs disappeared in a surprisingly short time. There was no spreading to the other leg nor any pulmonary embolisms. The patients could leave their bed after 4 to 5 days. In addition to early heparin treatment, Bauer advocated free active movements, undoubtedly a detail of vital importance. Movements of the legs were started almost immediately, and as soon as the acute symptoms disappeared, the patient was allowed to sit in a chair or to get up.

During the past 6 years Bauer has treated with heparin every patient in his clinic with deep venous thrombosis or pulmonary embolism. He had 258 cases. There were 3 deaths; the expected mortality was about 50. The patients stayed in bed an average of 4.6 days. Before the use of heparin in the treatment of thrombosis patients with thrombosis stayed in bed an average of 40 days. The results obtained by Bauer are shown in Table I.

In spite of the successful results in the series of cases reported in 1940 by Bauer, Clason, and others, in Sweden we still had to fight the advocates of conservatism for several years. In many hospitals the physicians in charge could be persuaded to use the new anticoagulant therapy only under pressure of the facts collected in the meantime. Many of them were afraid that hemorrhages might occur during heparinization. Some were afraid that heparin would cause detachment of thrombi, thus giving rise to pulmonary embolism.

The influence that the anticoagulant therapy had on the mortality rate in the different clinics as regards thrombosis and pulmonary embolism is shown in Table II.

In 1945, Zilliacus analyzed the effect of the introduction of the new principles of treatment as expressed in the mortality rates in thromboembolism, confinement to bed, and disabling sequelae of deep venous thrombosis in the legs. He studied the case reports of 1,158 cases of thrombosis among 256,282 patients from 20 Swedish clinics during the period 1940–1944. In this material every fourth case did not receive any specific treatment, while the remaining cases were regularly treated with anticoagulants. Zilliacus paid particular attention to the sequelae of thrombosis and therefore made a follow-up examination on all the patients, previously treated for thromboembolism, who could be traced.

In the conservatively treated cases with peripheral leg thrombosis the average time re-

quired for treatment, counted from the appearance of thrombosis, was 36 days or more than 5 weeks, and the temperature was above normal for 23 days. For the specifically treated series the period of incapacity was from 8 to 10 days and the temperature was above normal for 6.8 to 10 days.

Of 214 conservatively treated cases, 20 patients, or 9.4 per cent, died, while among 576 specifically treated cases in only 3 cases was the outcome fatal, 2 of them 8 to 12 days after starting the heparin treatment. If early and late attacks of embolism occurring before the start and after the finish of the treatment are also included, pulmonary embolism occurred in 34 per cent of the conservatively treated cases and in 7.6 per cent of the patients given specific treatment. Only 1.4 per cent of the patients in the last group showed an embolism during the course of the treatment, and only 1 patient died. It is therefore evident that the anticoagulant therapy does not increase the risk of the occurrence of pulmonary embolism; on the contrary it almost completely prevents new embolic attacks.

Thrombosis progressed to the other leg in 31 per cent of the patients in the conservatively treated group, but in only 2.2 per cent of the cases receiving anticoagulants.

Besides these 790 cases of deep venous thrombosis in the leg, the material included 280 cases of sudden pulmonary embolism without other signs of thrombosis. These were arranged in three groups: (1) immediately fatal cases, 114; (2) conservatively treated cases, 63; (3) cases treated with heparin or dicoumarol, 103. As regards group 1, it can be mentioned that at the postmortem examination newly formed thrombi were found in deep veins of the leg in not less than 60 cases while in 26 cases these veins were not examined. Many of these cases could certainly have been diagnosed and the patients saved. Twenty-one of the 63 conservatively treated patients in group 2 died, some of them after repeated attacks. None of the 103 patients in group 3 died. Seventy-one were treated with heparin and 16 with heparin and dicoumarol.

The results so far obtained of using heparin or heparin in conjunction with dicoumarol in the Swedish clinics are summarized in Table III.

TABLE III.—RESULTS IN SWEDISH CLINICS OF HEPARIN OR HEPARIN AND DICOUMAROL

	Cases of thrombosis or pulmonary infarction Bauer, Zilliacus	Deaths	Per cent
Conservative treatment	543	88	16
Heparin	769 } 900	5 } 6	0.67
Dicoumarol	131 }	1 }	

To these numbers can be added 371 cases of thrombophlebitis of the deep veins and 149 cases of pulmonary embolism, a total of 520 cases of thromboembolism reported by Murray in 1946[1] to have been treated with heparin. No deaths occurred in these series.

Dicoumarol has already been used on an extensive scale in Scandinavia and in this country. Recently Barker[2] and his associates at the Mayo Clinic reported on 292 cases of postoperative pulmonary embolism and 280 cases of postoperative thrombophlebitis in a total of 572 patients treated with dicoumarol, with only 11 cases with subsequent pulmonary embolism and among them only 1 fatal case.

The results in using anticoagulant therapy are therefore as striking as any hitherto reported following the introduction of a specific therapy in medicine.

SEQUELAE

With early diagnosis and regular treatment with anticoagulants, there is practically no mortality from diagnosed, uncomplicated thrombosis of the leg or from pulmonary embolism which is not instantaneously fatal. Failure to prevent death or spread of the process to the thigh or to the other leg may in most cases be attributed either to failure to diagnose or to defective treatment.

In Bauer's material the difference as to the sequelae between the mild and the severe cases of thrombosis was as follows:

In the 76 cases in which the popliteal vein had been saved, 60 suffered from no discomfort whatsoever on follow-up examination, and 16 showed an insignificant swelling in the calf only. Of the 27 cases in which the thrombosing process had reached the popliteal vein before treatment with heparin was begun, 14 cases

[1]Murray, G. Surg. Gyn. Obst., 1947.
[2]Barker, N. W. Minnesota Med., 1946, 29: 778.

TABLE IV.—THE FREQUENCY OF THROMBOSIS AND EMBOLISM AFTER SURGICAL OPERATIONS AND CHILDBIRTH IN PATIENTS ALLOWED FREE MOBILITY AND EARLY AMBULATION

Author	Place	Years	Surgical cases	Thrombosis		Fatal pulmonary embolism		
				Number	Per cent of the whole material	Number	Per cent of	
							Thrombosis	The whole material
Johansson and Holmdahl	Gothenburg	1933–1944	45,376	246	0.54	83	34	0.18
Westerborn	Gothenburg	1931–1944	43,737	254	0.56	56	22	0.13
Ekblom	Stockholm	1940–1944	19,000	143	0.75	30	21	0.16
Felländer	Örebro	1932–1941	36,489	226	0.62	52	23	0.14
Zilliacus	Stockholm	1940–1945	126,524	646	0.51	132	20.4	0.105
Dahl-Iversen	Copenhagen	1942–1944	1,736	10	0.58			
Koller	Zürich	1938–1942			About 0.5			

only were quite without discomfort. The 13 remaining had symptoms in the leg. All suffered from swelling of the lower part of the leg, in most instances moderate to severe. Five had in addition swelling of the thigh, 3 had severe pain and a feeling of heaviness in the leg.

At Bauer's clinic, where all cases except those with thrombosis diagnosed before their arrival at the hospital received early heparin treatment, the process did not progress beyond the calf in 80 per cent of the cases and it stayed in the calf in all cases where heparin was given before a phlegmasia had developed. From Zilliacus's data on conservatively treated cases, it appeared that thrombosis spread to the thigh in 80 per cent of the cases. In his series of cases treated with anticoagulants—the cases presumably were not treated in the most efficient manner as far as early diagnosis and therapy were concerned—the process spread to the thigh, in spite of the specific therapy, in 55 per cent of the cases.

It was noted by Zilliacus that when the thrombosis had extended to the thigh there was little difference between the conservatively treated cases and those treated with heparin. Swelling of the calf with discoloration induration with large varicose veins were present in most of the cases of both groups. Ulcus cruris occurred in 11 of 154 cases treated with heparin and submitted to follow-up examination. The result in this group was the same as that among the conservatively treated cases. An important difference, however, as compared with the conservatively treated cases, was that bilateral symptoms occurred only in 3 cases instead of in 33 per cent as found among the conservatively treated cases.

The sequelae in the patients with thrombosis of the calf who were treated with heparin were generally mild. Of 130 such cases 66 were completely free from symptoms, while the remaining patients showed only swelling of the calf after exertion. Only 1 patient in this group suffered from ulcer of the leg.

The specific therapy had, thus, in cases in which the thrombosis remained localized to the calf, permanently saved the patients from a chronic, painful, more or less severe, disablement.

THE TECHNIQUE OF ADMINISTERING HEPARIN

In most of the Swedish clinics heparin administration is started as follows: 350 to 450 milligrams a day are divided into four intravenous injections which are given at 8:00 a.m., 12:00 m., 4:00 p.m. and 8:00 p. m. or 10:00 p.m., in amounts of 125, 100, 100 and 125 milligrams. On the third day, the dose is lowered, e.g., to 300 to 350 milligrams. In case dicoumarol is given on the first day heparin is omitted as soon as an appropriate prothrombin level is reached. The same scheme is followed even in case of an acute pulmonary embolism. The use of dicoumarol alone is not permitted because it has repeatedly been observed that thrombosis in the calf proceeds to the thigh in spite of dicoumarol treatment. In fact heparin treatment has aborted the disease before the full action of dicoumarol

has evolved. Patients are consistently asked to move about in the bed as much as possible even on the second day and early ambulation is routine. Thus the average time in bed in Bauer's series was 4.6 days and in the other Scandinavian series 1 week to 10 days instead of 5 to 6 weeks as found in the series of patients treated conservatively.

Treatment now varies under different conditions. In small hospitals where no prothrombin analyses can be made only heparin is used. The time of coagulation of the blood is as a rule not determined. There seems to be a very small risk in using heparin without blood analyses. As to the use of heparin the contraindications seem to be very few. The risk of hemorrhages occurring is minimal. Hemorrhage is to be considered in the prophylactic treatment of postoperative cases but it has proved to be very insignificant in the ordinary treatment of leg thrombosis and pulmonary embolism.

OTHER THERAPEUTIC MEASURES

The question arises whether similar results as those reported here also could be obtained by other means, such as through active movements and early getting up from bed, sympathetic block causing vasodilatation in the leg, and surgical ligation of the larger veins.

It is evident that exercises under medical supervision and the early getting up of patients can reduce the incidence of thromboembolism. The incidence of thrombosis can be reduced to about 0.6 per cent in surgical clinics as is evident from Table IV.

Even in the Scandinavian series the mortality rate in thrombosis is still about 20 per cent, the same figure as that found at the beginning of this century in the surgical clinics of Germany and Austria as well as at the Mayo Clinic in this country during recent years. Consequently, there is a need for specific therapy.

The principles to be applied will at least partly depend upon the prevailing conditions. Venous ligation has in larger surgical units in this country given extraordinarily good results. In clinics, where the prothrombin level of the blood can be adequately followed, dicoumarol has been used either alone or in conjunction with heparin. In all smaller hospital units, like that of Bauer in Sweden, heparin treatment can be applied successfully. It is in fact to be resorted to in every case of early peripheral leg thrombosis and in acute pulmonary embolism.

The relative value of the different methods for the treatment of peripheral leg thrombosis or pulmonary embolism will of course become the subject of closer study during the next 5 to 10 years. At present we can confine ourselves to the statement that physiology and biochemistry have given us specific means which are highly effective in the treatment of thrombosis.

THE TREATMENT OF CHRONIC NONTUBERCULOUS PULMONARY ABSCESSES BY HIGH VACUUM SUCTION DRAINAGE

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DURING the past few years there has been progressive improvement in the management of chronic pulmonary abscesses. Lobectomy or occasional external drainage is now being employed with excellent results. It is felt, however, that in some well selected cases equally good results might be obtained by simpler means.

Often simple external drainage will fail and lobectomy, despite the excellent results, remains a formidable procedure which may result in the loss of some functional pulmonary tissue, which demands much of the time and energy of a skilled thoracic surgeon, an experienced anesthesiologist, and a trained surgical team as well as the services of a blood bank. No time need be spent, therefore, in advancing the desirability of a simpler method of treatment.

The purpose of this brief communication is to describe what may be such a method of treatment for certain carefully selected cases of chronic pulmonary abscess. To date, it has been employed in only 10 cases, but the results in all in which the method has had a fair trial have been so good that it seems justifiable to place the small series on record, in the hope that other surgeons may be encouraged to test the method and that a group large enough to be of statistical significance may be accumulated for analysis within a reasonably brief period of time.

The method proposed is an application of the continuous high vacuum suction drainage described by Neville in 1939 for the management of chronic empyema thoracis. He was confronted with a patient slowly wasting away with chronic empyema of 2½ years' duration. Within 4 weeks after thoracostomy and the institution of high vacuum suction drainage, the previously extensive empyema cavity had been reduced to a straight tract the size of the drainage tube, and within 7 months the patient had returned to work and was apparently completely well.

When this method came to my attention shortly after it had been described, it struck me that it might be useful in certain types of pulmonary abscess which in chronicity and other respects could be considered analogous to chronic empyema. The validity of the method as applied to chronic pulmonary abscess seemed enhanced by a careful study of pulmonary lobes resected for this cause. In some of these cases the conclusion seemed warranted that a cure might have been obtained by simpler means, with greater economy of time and personnel, with conservation of pulmonary tissue, and with less risk to the patient.

The term chronic in this connection is used to designate that type of pulmonary abscess which has existed sufficiently long to show roentgenologically a definite fibrous tissue capsule. Not all observers, of course, would agree with this definition, but as the basis of selection of cases for high vacuum suction drainage, it is an entirely adequate point of departure. If the zone of surrounding fibroplastic tissue is slight, as in the type of abscess which in some quarters might be termed subacute or even acute, the abscess is given the opportunity to heal spontaneously, or simple external drainage is employed. If, on the other hand, a considerable degree of lobar fibrosis and bronchiectasis is present, lobectomy is regarded as indicated.

The selection of cases for this method of treatment rests on still other criteria. The abscess must be single. It must be peripherally

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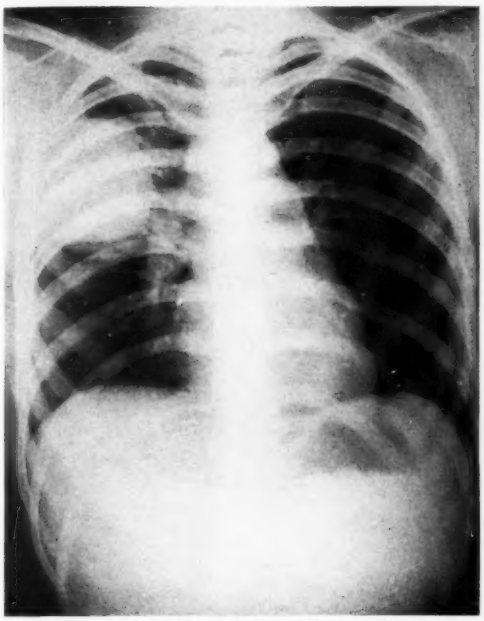

Fig. 1. Roentgenogram taken prior to operation revealing a spherical mass peripherally placed in the lower part of the upper lobe and in contact with the parietal pleura.

Fig. 2. Lateral projection corresponding to Figure 1, showing the lesion to occupy the posterior part of the upper lobe.

located. A pleural bridge must exist, so that satisfactory external drainage can be instituted without traversing the pleural space. If malignancy is a possibility, and if the usual diagnostic measures do not absolutely exclude it, exploratory thoracotomy and biopsy must be carried out. Finally, the lesion must be observed sufficiently long to make certain that the cavity is not decreasing in size spontaneously or under conservative methods of treatment. If these various criteria are met, the case is regarded as suitable for high vacuum suction drainage.

The operation is preferably done under intercostal nerve block. If preliminary aspiration reveals the existence of an adequate pleural bridge, the lesion is approached directly. If there is doubt regarding, or definite evidence against, the existence of such a bridge, exploratory thoracotomy is carried out by way of a small, strategically placed incision and the site of the skin incision for drainage is determined by the location of the pleural bridge. If no bridge is found, the method of treatment contemplated must be discarded in favor of lobectomy.

The abscess cavity is entered after resection of a small segment of overlying rib, and a drainage tube of appropriate size is inserted and made air-tight by the use of flanges and sponges. Patent bronchial openings in the walls of the cavity are fulgurated, but if this procedure be necessary, suction drainage is not instituted until they have closed.

Neville described the machine which he had devised for his patient, but in hospitals equipped with built-in suction systems no special machines are necessary. The suction apparatus is set at between 5 and 10 inches of mercury and the level is decreased only if the patient complains of a sense of severe pulling in the chest or if hemorrhage of serious degree occurs. The routine described by Neville is carried out with minor modifications. Thoracoscopic inspections of the cavity are made at weekly intervals and the measurements are

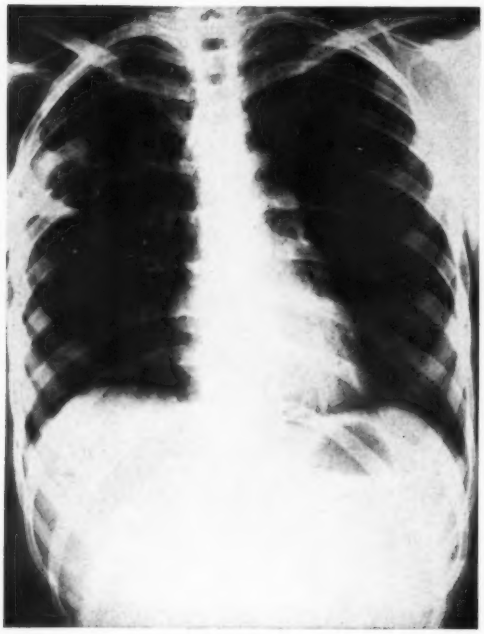

Fig. 3. Roentgenogram taken after operation shows the drainage tube passing through the resected segment of the fifth rib and the decrease in density of the lesion following suction therapy. The abscess cavity previously invisible is now quite apparent.

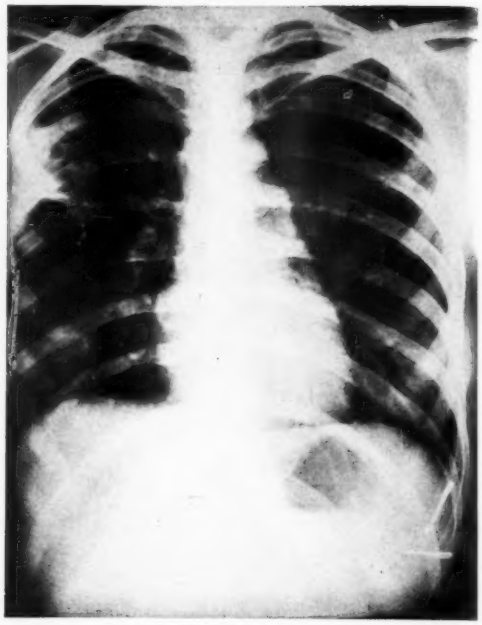

Fig. 4. At the time this film was taken the tube had been removed although the film indicates that a cavity may still be present. This is due to the peculiar arrangement of the fibrous tissue remaining in the upper lobe. The cavity has been observed fluoroscopically to flatten out against the parietal pleura and become obliterated. This patient has been asymptomatic for over 2 years and bronchograms reveal no abnormalities.

recorded at the same time for comparative purposes.

As soon as the patient is sufficiently improved to leave the hospital, he is instructed in the use of a small suction machine (available on rental from a commercial firm) which is similar to the standard tonsillectomy suction machine but is mechanically superior. It is capable of maintaining high vacuum suction for prolonged periods, with only brief intervals of nonoperation for the purpose of cooling the motor. The patient returns at intervals as necessary for observation until the abscess cavity is obliterated.

In every case in which a patient was treated by this method the clinical course has been the same. Following closure of the fulgurated bronchial orifices, if fulguration has been necessary, and the institution of high vacuum suction drainage, the size of the abscess cavity decreases rapidly and striking changes occur in the granulation tissue lining it. Previously pale and edematous, it rapidly assumes a healthy appearance and many new blood vessels are observed. The sites of the bronchial openings gradually disappear and the medial wall of the cavity approaches, and finally flattens out against, the parietal pleura. This important development in the healing process is hindered when the cavity is packed but is encouraged by the suction method of treatment.

In about half of these cases suction was discontinued for periods of as long as 2 weeks, as a control measure. Invariably the diminution in the size of the cavity, previously progressive, was halted, and was not resumed until suction was reinstituted.

The 10 patients in this series ranged in age from 20 to 65 years, every intervening decade being represented. The duration of illness prior to treatment had ranged from 3 to 12 months. Suction drainage was necessary for

an average of 3 weeks. In no instance in the series did it fail to bring about prompt decrease in the size of the cavity, eventual complete obliteration, and corresponding improvement in the condition of the patient. No untoward results of any kind have been connected with its use. The earliest of the cases has been followed for a 2 year period, and all other patients have been followed for at least a year. During the period of observation there has been no recurrence in any case though, because of the short time interval since treatment, the possibility of recurrence cannot be entirely discounted. Roentgenologic examination after obliteration of the abscess cavity has revealed in all cases persistence of shadows indicative of residual fibrosis.

Although the present series, as stated, consists of only 10 cases, the results secured seem to justify this preliminary report, chiefly because it is hoped that others will test high vacuum suction drainage in chronic nontuberculous pulmonary abscess and will report their results.

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RATE OF GAIN IN STRENGTH IN SUTURED ABDOMINAL WALL WOUNDS

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IN recent years a great deal of attention has been given to early ambulation following laparotomy. The strength of a wound immediately following the placement of sutures depends primarily on the total number of sutures which have been placed and upon the ability of the tissues to hold the sutures, as well as the tensile strength of the suture material employed and the manner of placement of those sutures. A review of the literature on wound healing yields very little reference to the rate of strength gain across incisions through the rectus muscle and fascia following approximation of the muscle and fascia with interrupted silk sutures. In the present study our objective is the determination of the amount of healing at different periods of time by measuring the tensile strength of the healing wound with nonabsorbable sutures remaining in place.

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According to Howes and Harvey, the rate of strength gain in a healing wound resembles the curve of growth in general (4). There are 2 periods in the strength gain of a healing wound; the first, the so-called "latent period" (2) lasts from 3 to 5 days. In the second period of the curve of normal healing, strength increases rapidly, and this phase continues until the wound is completely healed. Microscopically this period is associated with the process of fibroplasia (5).

METHODS

For the purpose of this experiment, commercially raised, healthy white rabbits were employed. These rabbits were maintained throughout the experiment, on a stock rabbit diet consisting of rabbit pellets and water. They were kept on this diet both before and after operation, and no attempt was made to add or subtract any dietary factor which would enhance or hinder the process of wound healing. Also, no attempt was made to choose a uniform size, weight, or sex. Both medium and large healthy rabbits were employed.

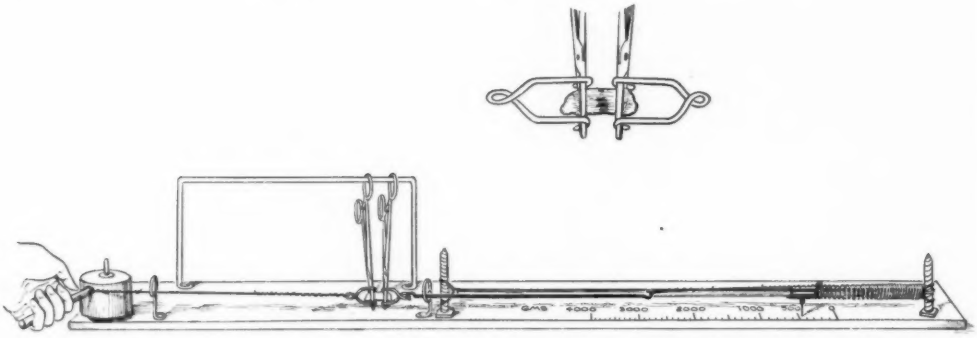

Fig. 1. Tensiometer employed for determination of strength of tissues. The strip of tissue to be tested is gripped in two forceps which remain perpendicular to the line of tension. The tension is slowly increased by turning a large spool connected by a wire to one of the forceps on the tissue. The other forcep is attached by a wire to the coil spring. A rider point is moved over the calibrations along a guide bar by the stretching of the spring, and remains at the point of maximum tension. Control tissues regularly ruptured midway between the clamps.

The rabbits were anesthetized by the injection of a necessary amount of aqueous sodium pentobarbital into the marginal vein of the ear. Roughly 35 milligrams of the drug were used per kilogram of weight. The hair was removed from the abdomen with barium sulfide and the skin washed thoroughly with water to remove all traces of the chemical. No marked skin reactions were observed from the use of the barium sulfide as a depilatory. Skin sterilization was obtained by the use of Novak's solution (6), and sterilization was maintained by the use of sterile towels as drapes around the operative field. Rubber gloves were not worn during the operation, but operations were preceded by a 10 minute scrub with soap and water followed by rinsing in aqueous zephiran solution. Surgical instruments, heat sterilized prior to the first operation of the day, were kept in a solution of aqueous zephiran 1:1000 between cases. The No. 000 and No. 0000 black silk (Deknatel) used for closure was autoclaved at 250 degrees for 10 minutes. All suture material was new, and none of it was autoclaved more than once.

A midline skin incision, roughly 14 centimeters long, was made beginning at a point just below the xiphoid process and carried down to the lower midabdomen. This incision exposed the linea alba. At this point the superficial fascia was separated either to the right or to the left of the midline and one anterior rectus sheath was exposed. An 11 centimeter incision was then made through the midanterior rectus sheath, rectus muscle, posterior rectus sheath, and peritoneum, usually about 1 centimeter from the midline.

The closure of the rectus incision was made by interrupted sutures; No. 000 silk was used in some rabbits, and No. 0000 silk was used in others. The anterior rectus sheath, rectus muscle, posterior rectus sheath, and peritoneum were all included in interrupted through-and-through stitches placed at regular 5 millimeter intervals. The bite included 2 millimeters of tissue on each side, and knots were tied with one square knot just tight enough for apposition without blanching. The skin was closed by means of a continuous suture of black cotton.

The rabbits were studied at varying times during their periods of wound healing. Some were sacrificed immediately, and their wounds measured for tensile strength, others were sacrificed at 24 hours, 48 hours, 72 hours, 5, 7, 9, 11, 15, 21 days and 6 weeks. No fewer than 6 rabbits were used for any single period's determinations except 9 days, and as many as 18 rabbits were used for some. In all, a total of 128 rabbits was used in this series, roughly 20 to 24 determinations were made on each rabbit, a total of roughly 2400 separate observations in all.

The rabbits were killed by the intravenous administration of 10 to 15 cubic centimeters

TABLE I. — TENSILE STRENGTH OF SILK-SUTURED ABDOMINAL WOUNDS IN RABBITS

Ratio of strength of wound to strength of previously undisturbed side

Healing period	No. of rabbits	Mean ratio per cent	Standard deviation
Statim	10	41.9	4.0
1 day	6	39.9	4.1
2 days	6	38.0	3.9
3 days	17	42.1	5.5
5 days	6	53.6	4.1
7 days	14	64.9	7.3
9 days	4	75.0	4.9
11 days	18	68.8	5.3
15 days	17	78.9	5.4
21 days	14	81.4	6.4
42 days	16	81.3	4.5

N.B. The absolute tensile strengths of the control sides varied from rabbit to rabbit, but was fairly consistent in the multiple tests in each animal, these variations not exceeding 600 grams and being regularly obviously associated with inequalities in the widths of the strips as cut. Use of the mean value in each animal was felt to correct for such inequalities in width. The absolute values varied in the control sides between 1500 grams and 4000 grams per cm. in different rabbits.

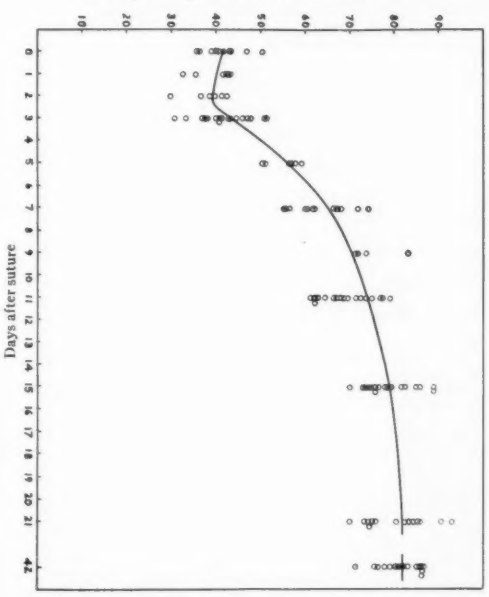

Fig. 2. The tensile strengths of silk-sutured abdominal wounds in rabbits at various periods after repair. The smooth curve passes in most instances within 0.6 times the standard deviation from the mean from the average for each time period, and in all cases within the width of the standard deviation from the mean.

of air. Immediately after the animal had expired, the skin was stripped from the abdomen. Careful note was made, at this time, of the presence or absence of any serous, bloody, or purulent accumulation near or on any of the wounds of the rectus muscles, also any gross evidence of stitch infection.

Next, the entire abdominal wall was excised and placed on a moist towel to prevent drying. This block of tissue was pinned to a cardboard beneath the towel to prevent the specimen from slipping during the process of sectioning into strips. The tissue was then cut into strips 1 centimeter in width, each strip running across the midline through the intact rectus muscle on the opposite side as well. Thus, each strip of tissue consisted of a portion of the rectus wound with two silk sutures in place, linea alba, and the previously undisturbed rectus on the opposite side, the entire transverse piece being 1 centimeter in width and about 4 centimeters long. Using a modified suture testing device (1), tensile strength on each side of the midline was tested. The mean tensile strength of the sutured portions in each rabbit was divided by the mean tensile strength of the previously undisturbed portions to determine the per cent tensile strength of the wound. Usually 10 determinations were made on each side of each rabbit. Between 4 and 18 rabbits were tested for each period's determinations. An average of all percentages was taken for all the rabbits tested at a specified period, to plot the curve of wound healing.

Where there was any evidence of gross infection or abnormal appearance of the wound, the rabbit was not used in the series. Microscopic sections of all wounds tested were made and studied. Here too, when there was any evidence of infection or variation from normal wound healing, the determinations were not included.

Tensiometer. We were unable to find in the literature a description of a tensiometer adequate for our purposes. One was therefore devised on the basis of the general principle employed for the suture testing apparatus

previously reported by one of us (1). A stout spring is stretched by tension on the strip of tissue to be tested. The rupture tension is recorded by a free rider which remains at the point of maximum tension after rupture has occurred (Fig. 1).

At the conclusion of these experiments a tensiometer of German make was found described in Sandblom's paper (8) on skin healing. It has the added factor of constant rate of increase of tension prior to rupture, and is therefore probably superior to the one we have used.

RESULTS

The first difficulty encountered was wound infection. Routine gross examination of wounds and microscopic examination of one segment of each wound resulted in the discard of 17 animals on this basis and 1 on the basis of hemorrhage into the wound.

It was found possible to construct a smooth curve of strength gain which falls well within the limits of the standard deviations from the mean value for each time period (Fig. 2, Table I).

At the completion of closure, the wound with sutures present was 41.9 per cent as strong as the previously undisturbed opposite side. This value dropped very slightly during the next 3 days, and then rose sharply, approaching 80 per cent at 15 days and rising significantly no more after that point.

Certain variations in these results were found to attend variations in type of suture material, including catgut, and manner of placement. These are the subject of further studies by 2 of us (Carleton Nelson and John Fast), and will be reported in later communications.

CONCLUSIONS

1. The strength at varying periods of the healing wound plus the sutures employed is of paramount interest to the surgeon in the light of the present trend toward early ambulation.

2. In rabbits, the strength of the freshly silk-closed abdominal wall wound is about 40 per cent of the undisturbed opposite side and remains at this value 3 days. Thereafter, it rises steeply to about 80 per cent at 2 weeks.

3. In the 6 weeks of observation in rabbits, silk-closed wounds never regained full preoperative strength, remaining at about 80 per cent of that value.

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Fig. 2.

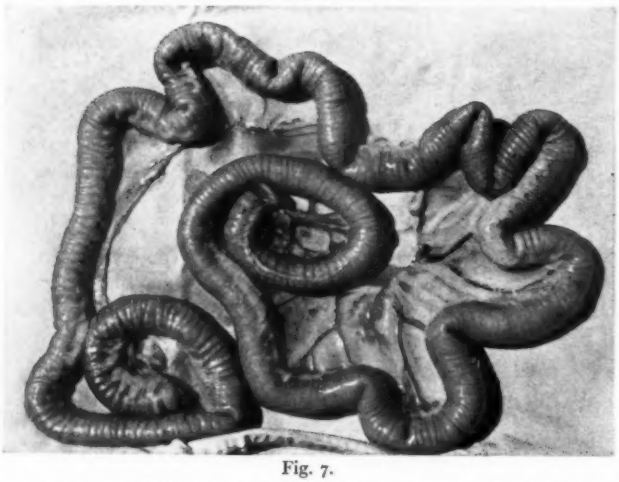

Fig. 7.

Fig. 2. Close-up kodachrome of a group of adhesions showing the agglutinated talc masses appearing as white flecks within the adhesions.

Fig. 7. Kodachrome of small bowel of a dog treated with powder No. 108. This shows the complete absence of any adhesions or any demonstrable inflammatory reaction.

Experiments with Non-Irritating Glove Powder.—C. Marshall Lee and Edwin P. Lehman

EXPERIMENTS WITH NONIRRITATING GLOVE POWDER

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SINCE the introduction of dry glove technique, now almost universally employed by surgeons everywhere, the powder used on rubber gloves has been under some degree of suspicion. But since any ill effect it might produce was masked by other more obvious factors such as infection, trauma, or suture material, it attracted comparatively little attention. The incrimination of lycopodium powder as the causative agent in many granulomatous lesions and intra-abdominal adhesions is now too well known to require detailed review. The historical aspects of this subject have been ably presented by Seelig, Verda, and Kidd (13). The use of lycopodium powder was rapidly abandoned in favor of magnesium silicate or talc. This inorganic material was thought to be physiologically inert in contact with living animal tissue and is now generally employed as a dusting powder for surgeons' gloves. With recognition of silicosis as an industrial disease entity, some interest was aroused in the possibility that talcum powder might not be entirely innocuous. In 1933 Antopol reported 2 cases of granuloma due to talc—one in the neck and one in the serosa of the appendix. These 2 cases were mentioned in passing in a report on lycopodium granuloma and the possibility was suggested that unrecognized talc granuloma might be quite common. Feinberg reported 2 cases of talc granuloma in 1937, and for the first time employed polarized light both to demonstrate and to identify the crystals responsible for the lesions. He injected small amounts of talc suspended in saline into three mice and produced granulomas, but no adhesions, and warned against the indiscriminate use of talcum powder in the operating room.

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Although scattered confirmatory reports (2, 4, 6, 10, 11) appeared in the literature, little attention was paid to them by clinical surgeons and in 1943 a second and quite comprehensive article by German (7) emphasized the danger of granuloma formation, but minimized the tendency to form intestinal adhesions. In 40 of 50 unselected patients who were subjected to a second laparotomy, German found intra-abdominal granulomas which he proved by means of polarized light to be the result of foreign body reaction to talc. Although there was a close parallel between the number of adhesions present and the number of granulomas, the adhesions were attributed entirely to collateral causes. He stated "In the mechanism of the formation of adhesions it is well known that fibrin plays an important part. The inability of silica *per se* to induce an exudation of fibrin would suggest that it is not important in the formation of adhesions. These observations would point to a very efficient mechanism for disposal of talc by the peritoneum."

German based his conclusions on the intraperitoneal injection of a 0.5 per cent saline suspension of talc into mice and on dry powder application in which he used only one test rabbit and one control rabbit, with and without trauma. He produced granulomas, but no adhesions. On this basis he concluded that "Talc *per se*, in the abdomen in the absence of injury to the peritoneum, is quickly removed from the peritoneal cavity, immobilized and covered with serosal cells, without the formation of an exudate, and without adhesions. Adhesions do not develop without some form of traumatization of the peritoneum sufficient to produce exudation of fibrin. Even in the presence of peritoneal trauma and exudation of fibrin, the talc plays a secondary rôle, in that it is caught up in the fibrin and is incorporated in the adhesions. Thus the developing granulomas may either add to the bulk and density of the developing adhesions or may

TABLE I.—POWDERS USED IN STUDY

		Flow and dusting qualities *Raw*	Flow and dusting qualities *Autoclaved*
1009-D	Regular amyloform (Containing 1 per cent bound HCHO)	+++	++
102	$POCl_3$ treated starch (Phosphorus oxychloride)	+++	+++
105	Calcium alginate	+++	++
106	HCHO treated starch (Containing about 0.3 per cent HCHO)	+++	++*
103	Raw corn starch	+++	+
104	Talc	+++	+++
103-A	Tantalum oxide	++++	++++
100	Corn starch derivative	+++	+++
101	Corn starch derivative	+++	+++
107	Corn starch derivative	++++	++++
108	Corn starch derivative	++++	++++

*Changes color to brownish tint.

impede the resolution of any adhesions once formed. In this sense it may be said to contribute to the disability produced by adhesions resulting from surgical operations."

It remained for Seelig (12, 13) to re-emphasize strongly the danger of talc as an adhesion producing agent. Although mice are notoriously recalcitrant to the production of adhesions, he was able to produce generalized adhesions quite uniformly in a large series (194 mice) in which 2 cubic centimeters of a 5 per cent saline suspension of talc was injected intraperitoneally. He tested some 24 different powders and selected potassium bitartrate as a nonreactive substitute. Later he employed a starch powder which was said to withstand autoclaving fairly well. This represents the first reported use of a starch derivative for this purpose, and our studies constitute an extension of Seelig's work with certain modifications in methods and materials.

In a comprehensive and detailed study Lichtman, McDonald, Dixon, and Mann have shown that talc is not an inert foreign body. They point out that commercial talcum is a mixture of talc, serpentine, dolomite, or tremolite. Talc itself is a hydrous magnesium silicate. "The material leached out of a talc crystal is not the same as the parent substance. The degree of hydration of this derivative substance determines its toxicity. For example a mole of alpha silicic acid may bind as many as 300 moles of water. The size, shape, and cleavage of a talc particle and its surface energy affect its so called solubility. In the body, alteration of the *p*H and the presence of protein in tissue fluids alter the size and characteristics of the dispersed aggregates." By means of the now common use of polarized light they conducted an extensive study of the pathogenesis of talc granulomas and adhesions, resulting from dispersed talc particles 0.5 to 10 microns in size.

The greatest barrier to the abandonment of talcum as a glove dusting powder has been the lack of an acceptable replacement for it. Many powders have been studied and the commonest single defect in those which are physiologically safe has been a tendency to gelatinize or agglutinate in the autoclave, thus defeating the primary purpose of the powder, namely to lubricate gloves and hands.

A further barrier to replacement of talcum powder has been a general failure fully to appreciate its danger. In most hospitals surgeons do not even take the precaution of washing the powder from their gloves before operating.

The purpose of our study was to verify the increasing evidence that talcum powder is a dangerous agent in human surgery and to evaluate certain proposed replacements for it.

EXPERIMENTAL STUDIES

Physical properties. Preliminary selective studies were made on the physical properties of ten powders, with commercial talc as the control.

The powders (Table I) used in this study were made available to us by the Department of Clinical Research, Ethicon Suture Laboratories, Division of Johnson and Johnson, New Brunswick, New Jersey. The first four powders have already been tried out by other investigators (7, 11) and were included for comparative purposes. The last four powders, designated 100, 101, 107, and 108 are derived from corn starch, which has been treated by physical and chemical means to prevent gelatinization in the autoclave. These four powders differ substantially only in degree of treatment, except that numbers 107 and 108 have

had a special chemical treatment to improve their lubricating value. The identity of the remaining powders in Table I is self-evident.

The fineness, and flow and dusting qualities of the raw powders were arbitrarily classified by gross estimation from + to ++++, the latter representing the greatest freedom of flow and ease of distribution in dusting gloves and hands. Samples of each were then autoclaved under 15 pounds of pressure for 15 minutes and retested. The results are shown in Table I.

Examination of these results shows that powders 100 and 101 were about comparable to talc and that powders 107 and 108 and tantalum oxide were superior, with respect to physical qualities after autoclaving. No experiments on tissue tolerance were conducted with the group of powders showing inferior physical qualities. Powder 107 was also eliminated because, since No. 108 was known to represent a further refinement of it, detailed study became an unnecessary duplication. Tissue tolerance studies were therefore conducted on powders 100, 101, 103-A (tantalum oxide) and 108, with talcum (104) as a control.

Method of testing peritoneal reaction. Dogs were selected as the test animals because actual operating room conditions could be closely approximated and because the peritoneal reactions of dogs more nearly approach human reactions than do those of mice, rats, guinea pigs, or rabbits which have been used in studies heretofore reported by others. In a further effort to duplicate operating room conditions, dry powder was used in open operation rather than by injection in a saline suspension.

In every operation the abdomen was opened through a standard rectus incision. Rigid aseptic technique was employed throughout, except that before beginning the operation both operator and assistant washed their gloves thoroughly under running tap water. In every operation the small bowel was "run" from Treitz's ligament to the ileocecal valve. When a powder was being tested it was dusted, as evenly as possible, over the bowel and both mesenteric surfaces as the bowel was run. When the last loop had been handled or treated the abdominal wound was closed in layers with silk.

TABLE II.

Equivalents in washings from operating room gloves	Weight in grams	Volume (In teaspoon measures)
2 pairs	0.26	1/8
4 pairs	0.52	1/4
8 pairs	1.024	1/2
16 pairs	2.04	1

After an interval of 3 weeks each dog was reopened, the same technique being used, and explored for adhesions. When few adhesions were found, a careful count of them was made after the method of Lehman and Boys (13). When adhesions were too numerous to count they were designated +++ or ++++, denoting generalized massive adhesions.

Quantity of test powder. In order to arrive at a suitable quantity of powder for test purposes, 4 pairs of gloves were drawn from the ready supply in the operating rooms of the University of Virginia Hospital. The outer surfaces of these gloves were washed as thoroughly as possible under a single washing with a fixed quantity of water.[1] The water was then evaporated and the residual powder was found to weigh 0.5262 gram. This was taken as the maximum amount of powder with which the peritoneal cavity might be contaminated by an operating team of four persons, if only one pair of gloves were worn by each, and if none of the gloves was punctured.

Since the powders to be studied were of different specific gravities a volumetric measure was considered better for comparative purposes. A set of kitchen teaspoon measures was employed and approximate values were obtained for talc (Table II).

One-half teaspoonful represents the amount of talc from 8 pairs of gloves. On this basis, in order to make the tests sufficiently rigorous, this amount was selected as the dose to be dusted over the peritoneum of dogs. Certain exceptions to this dosage will be noted under results.

Bacterial studies. Although it had already been shown that the physical properties of powder 108 were not impaired by autoclaving, it seemed desirable to establish that this

[1]It is of interest that when these washed gloves were air-dried they were still abundantly covered with a fine coating of powder.

Fig. 1. Small bowel of dog treated with talcum powder. The bowel and mesentery have been removed *en masse* and laid over the end of a bucket. Adhesions are so numerous and dense that the cohesive mass hangs together like a cap.

powder (which will be shown to have a high order of tissue tolerance) could, in fact, be effectively sterilized.

Through the courtesy of Dr. Frank Meleney's laboratory at Presbyterian Hospital, New York, some spore threads were obtained of a highly heat-resistant strain of Bacillus subtilis. This strain, when the test tube is completely surrounded by the water, will withstand boiling for 20 minutes.

A sample of powder 108 as received was autoclaved for 15 minutes at 15 pounds pressure. Culture from this sample was sterile.

A second sample was contaminated with heat resistant Bacillus subtilis spores and then cultured without autoclaving. Bacillus subtilis was readily cultured from the sample.

TABLE III.—CONTROL STUDIES—NO POWDER AND TALCUM POWDER

Type of powder	Amount of powder	Equivalent in glove washings	Number of dogs	Average number of adhesions	Greatest number of adhesions	Smallest number of adhesions
None	None	None	10	0	0	0
Talcum Powder	½ Tsp.	8 Prs.	10	++++	++++	++++
	¼ Tsp.	4 Prs.	5	++++	++++	++++
	1/16 Tsp.	1 Pr.	2	+++	+++	+++

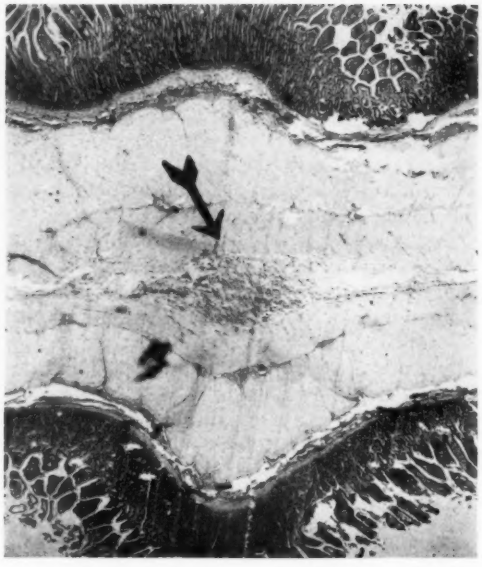

Fig. 3. Section under low power through an adhesion between two loops of bowel.

A third sample was similarly contaminated and then cultured after autoclaving. Culture from this sample was sterile.

RESULTS

Controls (*Table III*). No adhesions resulted when no powder was used. When talcum was used dense generalized adhesions were formed. Even when the dose of test powder was reduced to 1/16 teaspoonful, or roughly the washings from one pair of gloves, the result was the same.

These dogs were sacrificed and at autopsy the small bowel was removed *en bloc* and formed one cohesive conglutinate mass which, when draped over the end of a bucket, sat on it like a cap (Fig. 1). The small spots of agglutinated talc were readily visible in gross under the adhesions (Fig. 2, frontispiece). Microscopic sections taken through sample adhesions showed the talc embedded under the adhesions against the serosa (Figs. 3 and 4). Under polarized light the identity of this material was evident (Figs. 5 and 6). The celiac and superior mesenteric nodes were greatly enlarged. Sections of these were taken to de-

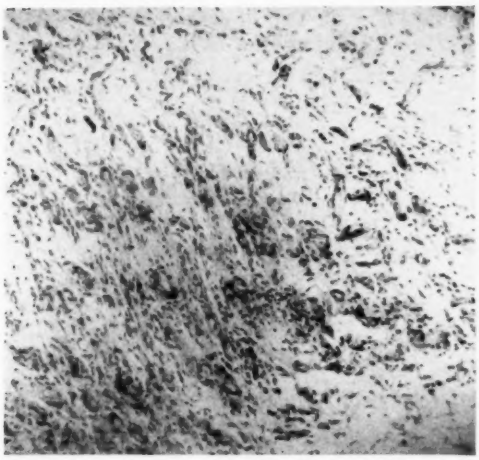

Fig. 4. Higher magnification of the area indicated by the arrow in Figure 3. This shows the inflammatory reaction and the numerous foreign body giant cells.

Fig. 5. The same area as shown in Figure 4, under polarized light with partial rotation of the prisms. This brings out the larger talc particles.

termine whether or not there had been any phagocytosis of the talc with deposit in the regional nodes. Under ordinary light these sections showed only the usual inflammatory lymphoid hyperplasia. Under polarized light exhaustive study showed only an occasional birefringent particle—an average of one to three a section.

Experiments (*Table IV*). Tantalum oxide produced as extensive adhesions as did talc. Further work on this powder was abandoned.

The results with powders 100 and 101 were encouraging and in the case of the latter sufficiently so to suggest testing the effect of an increased dosage. Two dogs were treated with a full teaspoonful of powder 101 equivalent to washings from 16 pairs of gloves. It is of interest that each of these dogs had been used in a previous series and the increased dose had been put in when they showed no adhesions after the first test. One dog showed no

TABLE IV.—EXPERIMENTAL STUDIES—TEST POWDERS

Type of powder	Amount of powder	Equivalent in glove washings	Number of dogs	Average number of adhesions	Greatest number of adhesions	Smallest number of adhesions
Tantalum oxide	½ tsp.	8 prs.	3	++++	++++	++++
Starch No. 100	½ tsp.	8 prs.	5	5.7	12 (+++)*	0 (1 dog)
Starch No. 101	½ tsp.	8 prs.	5	4.0	18	0 (3 dogs)
Starch No. 101	1 tsp.	16 prs.	2	2.5	5	0
Starch No. 108	½ tsp.	8 prs.	10	0	0	0

*One dog had an infected laparotomy wound and showed +++ adhesions. Because of this extraneous factor the average and greatest number of adhesions is taken from the remaining four dogs.

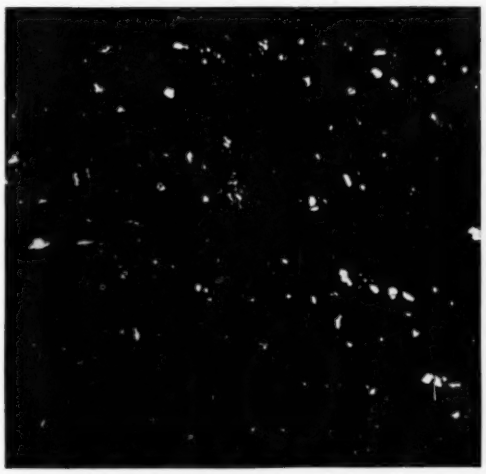

Fig. 6. The same area as in Figures 4 and 5. Here the prisms have been completely rotated blotting out all but the doubly refractile talc particles.

adhesions at his third laparotomy and the other showed only five. Since powder 108 was known to represent a further refinement in processing and since its physical properties were superior, the next major series was conducted with this powder. In every case, when the dog was opened after 3 weeks not a trace of powder was to be found, nor was there a single adhesion present. The bowel when removed *en bloc* was as clean and healthy as if it had never been touched (Fig. 5). These striking results indicate the superiority of powder 108 over every other powder tested and are as good as the controls without powder.

CLINICAL EVALUATION

By arrangement with the superintendent of a private hospital in this city powder 108 was installed in the operating room in place of talcum, without the prior knowledge of the surgeons working there. The operating room supervisor was asked to take note of any comment they might spontaneously make.

With only one exception every surgeon commented favorably, having noticed the improvement in physical quality over the powder previously in use, and asked what the "new powder" was. The single exception made no comment at all, favorable or unfavorable and apparently did not notice the change.

In the course of this trial use only one unfavorable feature was observed. It happens that in this particular hospital glove powder is put up in aluminum salt shakers and used throughout the course of a day's operating schedule. Frequently these shakers are not emptied in one day and are reautoclaved and used again the next day. It was noted that while the physical properties of the powder remained unimpaired through one, or at most two autoclavings there was some tendency to clump after the third such sterilization. After the fourth or fifth, although the clumps were readily "shaken out" and fine dusting powder could be obtained from the can, many residual lumps were left.

This single disadvantage seems trivial in comparison with the many advantages derived from the use of this powder, and is easily obviated either by using smaller shakers or by employing the widely used technique of putting up the dusting powder in individual packages with each pair of gloves.

DISCUSSION

It has been shown in our control studies that the atraumatic, aseptic manipulation and handling of the small bowel does not produce adhesions in healthy dogs.

When dry talcum powder is dusted over the serosal surfaces, massive, dense, and uncountable adhesions were produced wherever the talc came in contact with the tissues. This indicates that neither trauma nor infection are required, in the presence of talc, to produce adhesions and the powder alone must here be held responsible. This is in direct contrast to the observations reported by German.

Furthermore, our study of the regional lymph nodes indicates that, at least after 3 weeks, any effort on the part of the body to remove the powder via the lymphatics has been unsuccessful.

Our observations on the test powders indicate that powder 108 is completely absorbed from the peritoneum without any demonstrated inflammatory reaction and that it produces no adhesions whatever.

The fate of this powder does not offer any great pharmacological problem (3). Since it is a corn starch powder it is simply taken up by the peritoneum and metabolized like any ingested starch. Its advantage over raw starch and other treated starches is that its dusting, lubricating, and flow qualities are not adversely affected by autoclaving. Its superiority over talcum powder, tantalum oxide or any other mineral, metallic or nonmetabolized powder, is obvious.

MacQuiddy who has investigated the sensitizing propensities of this substance both in human patients and in animals, has failed to demonstrate, under experimental conditions, any sensitizing or anaphylactogenic properties. However, subcutaneous tissue sections obtained by MacQuiddy indicated that, in some instances at least, complete absorption of the powder had not occurred at the end of 56 days. In such cases, relatively large compacted masses (up to 200 mgm.) had been embedded, and under such circumstances absorption might be expected to be slow and

difficult. MacQuiddy's studies are being continued and will be reported in detail at a later date.

CONCLUSIONS

1. Further evidence is presented that talc is a deleterious substance in living tissue, that it produces a violent peritoneal reaction and dense adhesions, and that its use as glove dusting powder is dangerous.

2. A commercially prepared dusting powder is shown experimentally to have:

a. Excellent physical qualities of flow and fineness, unaffected by autoclaving.

b. Complete absorption by the peritoneum without inflammatory reaction and without the formation of adhesions.

c. Complete sterility under standard autoclaving procedure after known contamination with spores of a heat-resistant organism.

3. A brief clinical trial of this powder has been entirely satisfactory.

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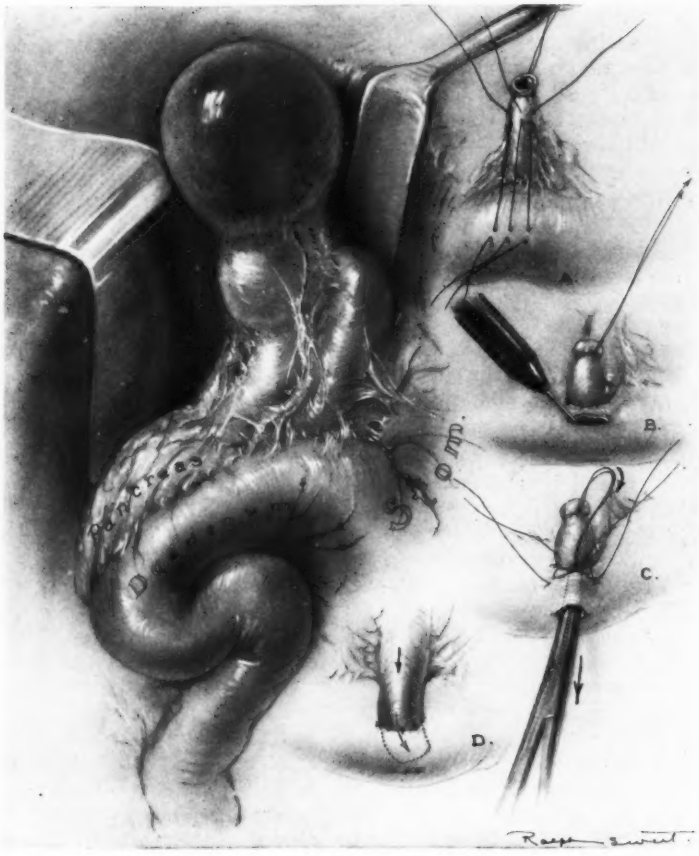

Fig. 1. Simple implantation of common bile duct. The duct is markedly dilated following previous ligation at junction of duct and duodenum. A, Posterior row of sutures placed. B, Incision made into lumen of intestine. C, Second incision made into duodenum. Hemostat placed through two incisions and ligature on duct grasped. D, The free end of duct 2 to 4 millimeters in length remains extending into lumen of intestine.

Experimental Implantation of the Common Bile Duct into the Intestine.—Frederick M. Binkley, Robert Palmer, and H. J. McCorkle.

EXPERIMENTAL IMPLANTATION OF THE COMMON BILE DUCT INTO THE INTESTINE

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CLINICAL and experimental surgical procedures in which the bile duct is implanted into the intestinal tract have been employed with increasing frequency in recent years. It is desirable that biliary intestinal anastomosis be done in such a manner as to prevent leakage of bile into the peritoneal cavity in the early postoperative period, and to avert the later postoperative complication of cholangitis which often is associated with stricture at the site of anastomosis, stasis and infection of bile, and probably with reflux of intestinal contents into the biliary duct system.

In consideration of these points several types of experimental implantation of the common bile duct into the intestine of dogs were performed in an attempt to develop an efficient, simple procedure.

The experiments were divided into four main groups:

1. *Simple implantation.* Choledochoduodenostomy was done in 13 dogs, 8 of which had a normal common bile duct. In the remaining 5 animals the common bile ducts were ligated at a preliminary operation. Two or 3 weeks later these animals were reoperated upon and the dilated common bile ducts were implanted into the duodenum.

The technique of implantation of the bile duct into the duodenum is illustrated in Figure 1. After the bile duct is ligated and dissected free a single row of interrupted cotton sutures is placed posteriorly, approximating the duodenum and the posterior wall of the common duct at a distance of 3 to 5 millimeters from the free end of the duct. The posterior row is tied under direct vision, in order to insure accurate serosa-to-serosa approximation. Two incisions are then made in the duodenum, one just anterior to the suture line, and with a curved hemostat, which is passed through the two incisions, the common duct is drawn into the lumen of the duodenum. An anterior row of interrupted fine cotton sutures is placed, completing the serosa-to-serosa anastomosis. The ligature is cut from the distal end of the duct, leaving a free end from 2 to 4 millimeters in length extending into the lumen of the duodenum. The second incision is closed with 1 or 2 interrupted cotton sutures.

In none of these animals was there evidence of leakage of bile from the anastomosis in the early postoperative period. The postoperative course was not remarkable except for the urinary findings. In most animals daily urinalysis revealed the presence of bile during the early postoperative period, but the urine invariably was free of bile by the 10th postoperative day. In order to determine the cause of the transient jaundice, 3 animals were sacrificed on the 5th postoperative day. In these animals the common bile ducts were found to be somewhat dilated. There was considerable edema at the site of anastomosis and in the surrounding duodenum. In all cases bile flowed spontaneously into the duodenum.

The remaining 10 animals were sacrificed from 34 to 338 days after the choledochoduodenal anastomosis (Table I). In these animals the anastomosis was found to be well

TABLE I.—SIMPLE IMPLANTATION

	Normal duct	Dilated duct	Total
Number of animals	8	5	13
Postoperative duration—days	5–338	55–313	
Results of anastomosis			
Satisfactory	6	4	10
Unsatisfactory	0	0	0
Mortalities[1]	2	1	3

[1]Causes of death: anesthetic, 2; peritonitis, 1.

From the Division of Experimental Surgery of the University of California Medical School. This work was supported by a grant from the Christine Breon Fund.

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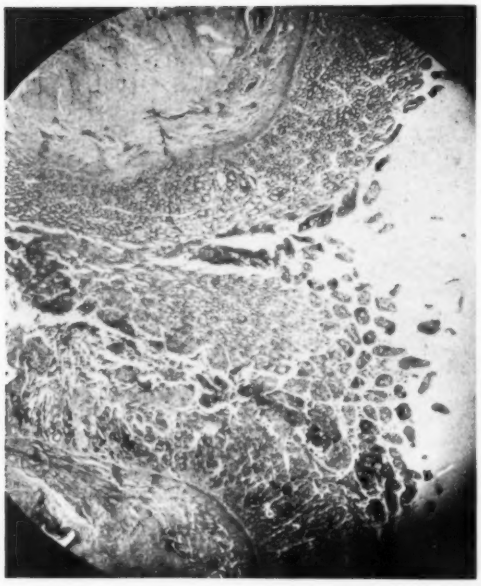

Fig. 2. Photomicrograph of anastomosis demonstrating mucosal junction of common duct and duodenum.

Fig. 3. Roentgenogram following simple implantation. Gastrointestinal series consistently failed to demonstrate regurgitation of barium or free air into biliary passages.

healed and appeared to be functioning satisfactorily. There was no evidence of stenosis. The mucosa of the common duct appeared to be continuous with the duodenal mucosa and the orifice usually lay between mucosal folds. Histological sections showed the ductal and duodenal mucosa to be directly continuous, and several histological sections revealed elevation of the duodenal mucosa about the stoma, forming a papilla-like structure. There was a minimal fibroblastic response, and no evidence of chronic inflammation (Fig. 2). X-ray studies failed to demonstrate regurgitation of barium or free air into the extrahepatic biliary passages (Fig. 3).

TABLE II.—SIMPLE IMPLANTATION INTO BLIND LIMB OF JEJUNUM

	Normal duct	Dilated duct	Total
Number of animals	4	1	5
Postoperative duration—days	5–126	67	
Results of anastomosis			
Satisfactory	3	1	4
Unsatisfactory	1	0	1
Mortalities[1]	2	0	2

[1]Causes of death: peritonitis, 1; cholangitis, 1.

There were 3 deaths in this group. Two were caused by an overdose of sodium pentobarbital used for anesthesia. One animal died with peritonitis on the 15th postoperative day but there was no apparent leakage of bile from the anastomosis. The origin of peritonitis in this animal probably was contamination with intestinal flora at the time of operation.

2. Simple implantation into blind limb of jejunum. In the second group of 5 animals the common duct was implanted into a blind limb of jejunum (the Roux arm principle being utilized), the same method being used as described for the first group of animals (Fig. 4). In dogs satisfactory fixation of the blind jejunal limb was difficult to obtain and the anastomoses were unavoidably under considerable tension. In 3 of the 5 animals results were satisfactory and the findings were similar to those described in the first group (Table II). There were 2 deaths. One animal died on the 3rd postoperative day with diffuse peritonitis;

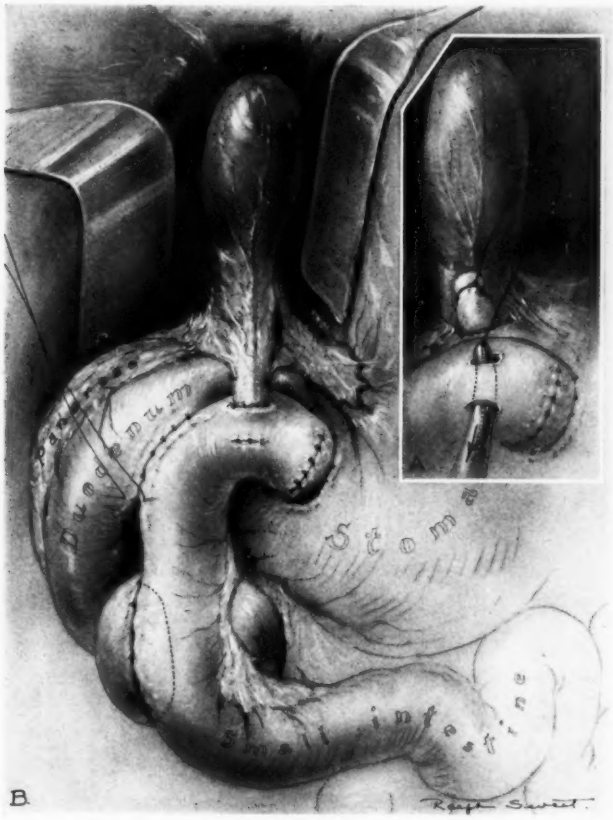

Fig. 4. Simple implantation into blind limb of jejunum. A, Simple implantation of duct. B, Completed procedure showing implantation into blind limb and end-to-side jejunal anastomosis.

the anastomosis was not healed and there probably was leakage of bile into the peritoneal cavity. The other animal died with acute cholangitis on the 5th postoperative day. The anastomosis was found to be healing satisfactorily with no leakage of bile. The bile ducts were filled with thick, mucopurulent exudate.

3. Anastomosis using mechanical support. In a group of 5 animals a dilated (previously ligated) common bile duct was anastomosed to the duodenum, over a mechanical support (Fig. 5).

In 2 animals the anastomosis was done over a rubber catheter, and in 3 a flanged tantalum metal tube was used. In the cases in which a rubber catheter was used, one dog was sacrificed on the 10th, and one on the 44th postoperative day (Table III). The anastomoses were well healed and appeared to be function-

TABLE III.—ANASTOMOSIS USING MECHANICAL SUPPORT

	Tantalum tube	Rubber tube	Total
Number of animals....	3	2	5
Postoperative duration—days.....	12–252	10–44	
Results of anastomosis			
Satisfactory.....	3	2	5
Unsatisfactory.....	0	0	0
Mortalities[1]	2	0	2

[1]Causes of death: multiple liver abscesses, 1; pneumonia, 1.

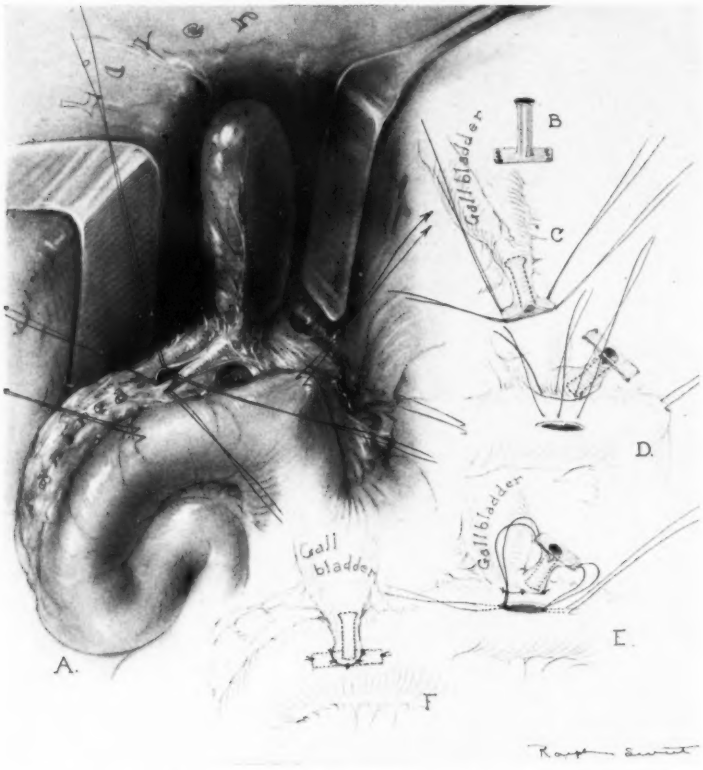

Fig. 5. Anastomosis over tantalum tube. A, Common duct dissected free and distal flaps constructed. B, Flanged tantalum tube. C, Duct flaps anchored to flanges of tube. D, Posterior row of sutures placed. E, Tantalum tube brought into lumen of intestine and anchored into position. F, Completed anastomosis.

ing satisfactorily. In one animal the duct wall was thickened and there were numerous adhesions and an increased amount of scarring about the anastomosis. Histological examination revealed a marked increase in connective tissue reaction and inflammatory response when compared with similar sections from implantations in groups I and II (Fig. 6). Two of the 3 animals in which a tantalum tube was used died, one on the 12th and one on the 30th postoperative day. The former was found to have peritonitis resulting from a perforation of one of numerous liver abscesses, and the latter died with pneumonia. In both animals the anastomoses were well healed and appeared to be functioning satisfactorily and the tantalum tubes had remained in their original positions. The third animal was sacrificed on the 252nd postoperative day, at which time the tube was found to have passed from the site of anastomosis through the intestinal tract. The anastomosis was functioning satisfactorily. However, the duct wall was thickened, and histological sections demonstrated an increased amount of connective tissue about the anastomosis with a moderate inflammatory reaction.

4. Anastomosis using reinforced fascial tube. In 3 animals the common bile duct was divided at its junction with the duodenum and the defect was replaced by a tube of viable fascia reinforced with a fine tantalum wire mesh. At a preliminary operation a rectangu-

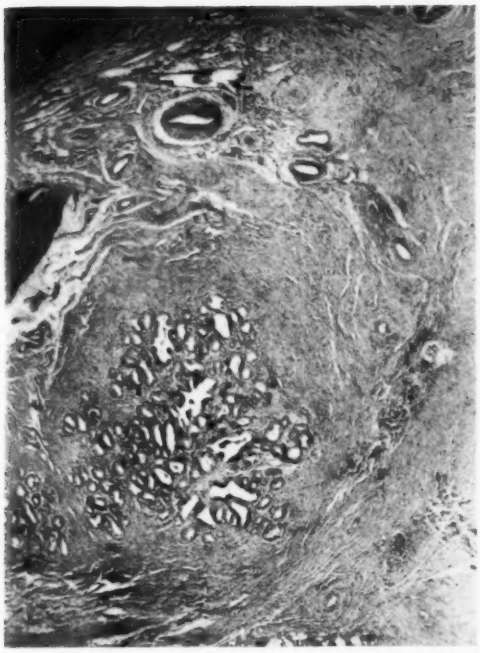

Fig. 6. Photomicrograph of area adjacent to anastomosis performed over rubber catheter demonstrating surrounding connective tissue reaction.

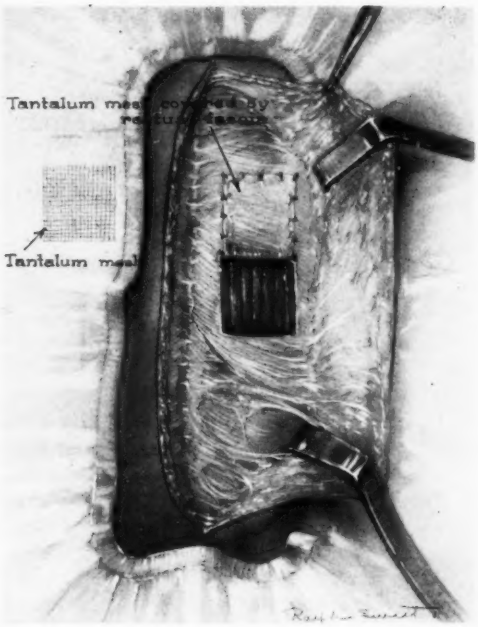

Fig. 7. Construction of fascial flap reinforced with tantalum mesh. Flap of rectus abdominis sheath turned back over square of tantalum mesh and sutured into position.

lar flap of rectus sheath was dissected free and folded back over a square of tantalum mesh placed upon the anterior surface of the rectus abdominis sheath and sutured into position (Fig. 7). In this manner the sheet of tantalum mesh was covered on its anterior surface by the flap of fascia and on its posterior surface by the anterior wall of the rectus sheath. Two to 3 weeks later this double thickness of fascia, reinforced with tantalum mesh, was excised and fashioned into a tube, which was then anastomosed at one end to a dilated common duct, and at the other end to the duodenum. The anastomosis was performed about a rubber catheter which was left extending into the duodenum and portions of omentum were brought about the anastomosis (Fig. 8).

These 3 animals were sacrificed at intervals varying from 119 to 251 days postoperatively (Table IV). At necropsy the anastomoses were found to be surrounded by abundant vascular adhesions. In all 3 animals the anastomoses were patent and appeared to be functioning; however, the extrahepatic biliary system was distinctly dilated. The rubber catheters were noted to have passed into the gastrointestinal tract. The tantalum mesh tube protruded into the lumen of the intestine for a distance of 2 to 3 millimeters and was almost entirely covered with duodenal mucosa. The tubes on being opened were found to be almost completely lined with mucosa; however, there were spotty areas through which the tantalum mesh was visible. A relatively thick fibrous wall surrounded the tube which

TABLE IV.—ANASTOMOSIS USING REINFORCED FASCIAL TUBE

Number of animals	3
Postoperative duration—days	119–251
Results of anastomosis:	
Satisfactory	3
Unsatisfactory	0
Mortalities	0

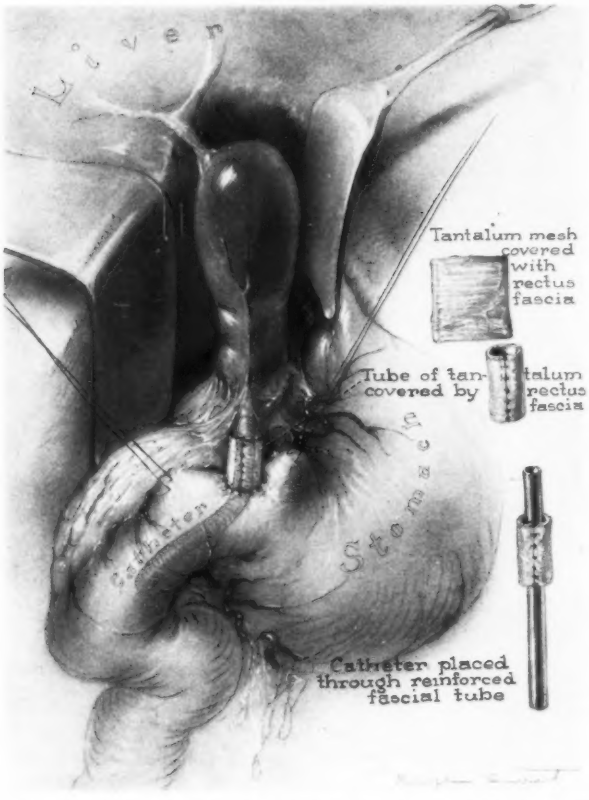

Fig. 8. Anastomosis utilizing reinforced fascial tube. End-to-end anastomosis of dilated common duct and fascial tube. Fascial tube anastomosed to duodenum over rubber catheter.

apparently was not constricted due to the presence of the tantalum mesh.

SUMMARY

1. A simple type of biliary intestinal anastomosis has been done in 18 experimental animals. It may be done rapidly and has given good functional results with minimum inflammatory reaction at the site of anastomosis.

2. Anastomoses employing a rubber or metal tube have been done in 5 experimental animals and these anastomoses invariably have exhibited evidence of considerable inflammatory reaction, scarring, and stenosis.

3. An experimental method for the replacement of a defect in the common duct of animals by a graft of fascia reinforced by tantalum wire mesh is described.

4. It appears desirable to use the simplest possible type of anastomosis (as described in group I) in situations where a sufficient length of the common duct remains to permit direct implantation of it into the duodenum. Use of the Roux arm principle may not be required in all instances, and might be limited to situations in which the presence or possibility of cholangitis is a factor.

5. The use of metal or rubber tubes for mechanical support in choledochointestinal anastomosis should be avoided if possible because of their tendency to produce marked scar tissue reaction with stenosis. However, it

is acknowledged that there are many situations where such support is essential. In such instances temporary support with a very soft rubber tube appears preferable to more permanent support with rigid metal tubes.

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PRINCIPLES INVOLVED IN SURGICAL THERAPY OF "ENCAPSULATED" FIBROSARCOMA OF SOFT TISSUES

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IT is an established fact that success in the treatment of any malignant disease depends to a great extent upon a knowledge of its origin and course. This means that the institution of adequate surgical measures based on this knowledge is just as important as the early recognition of the presence of the malignancy. Even though it is the pathologist's responsibility in the average instance to make the actual diagnosis of malignancy when the surgeon is in doubt, it is the surgeon who has undertaken the responsibility to effect a cure. Having undertaken this responsibility, it seems logical that he should be expected to possess as complete a knowledge as is practical concerning the pathological entity at hand. When this pathological entity happens to be a sharply delimited tumor found arising from the soft tissues of the body, that is, from the subcutaneous tissue, muscle or intermuscular fascial planes, the gross appearance of this tumor may lead to the impression of a relatively benign process before the pathologist has had an opportunity to declare himself. It is not too unusual that the same impression may be common to both individuals even after using the time-saving device of frozen section technique for histological study with the result that both are temporarily lulled into a false sense of security. Under such circumstances the definitive surgical extirpation results in a simple enucleation of an apparently encapsulated tumor from its bed of areolar tissue. The postoperative clinical impression in such instances agrees with the preoperative diagnosis of perhaps a fibroma until the permanent sections are examined by the pathologist. If the final diagnosis happens to be "fibrosarcoma of low grade malignancy," the surgeon is faced with the problem of considering the original surgery as being adequate or of choosing a waiting game. Since tumors spread in the human body only by actual dissemination of viable cells or are manifest in more than one part of an area through a multicentric origin, the correct decision in this instance will be dependent upon an accurate and full knowledge of the disease process.

From Division of Surgery, Northwestern University Medical School

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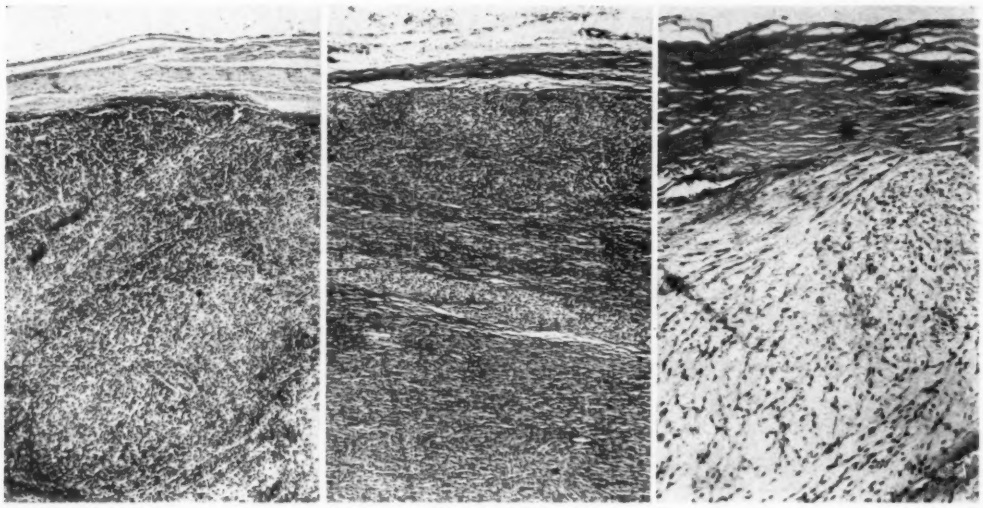
PATHOLOGY

The histological studies of the last few decades have made considerable progress in distinguishing among the various tumors once collectively known as "fibrosarcoma." In the course of this differentiation an expected amount of controversy has taken place among pathologists, out of which has arisen a fuller knowledge of the growth characteristics of



a b c

Fig. 1. Three examples of fibrosarcoma each of which presents a well defined fibrous capsule despite the variation in cellular structure of tumor. a, Highly cellular type; b, fibrous type; c, fibromyxomatous type.

these neoplasms. Many forms of spindle-cell sarcoma now prove on closer investigation to belong to groups of tumors arising from nerve structures, muscle, fat or synovial tissue. In other words, it now appears that practically all of the sarcomas of the soft parts are derived from specialized tissue cells and not from the supporting fibroblasts. The "fascial sarcomas of Virchow" thus remain as one of the few pure forms of fibroblastic sarcoma, even though modified by lipomatous or myxomatous degeneration, whereas an excellent example of this recent clarification is represented by the synovial sarcoma group. The synovial tissues are generally agreed to have arisen from mesodermal tissue, but they normally are composed of an endothelial layer and an outer fibrous layer. The tumors arising from this tissue thus fall into two microscopic types. The first are those arising from the inner layer and are more epitheloid in character while the second are those arising from the outer layer and are usually indistinguishable from the common fibrosarcoma. On the other hand, all gradations of specialized fibroblastic tumor formation now considered as of neural origin may be obtained by a complete study of the pathological possibilities found in von Recklinghausen's disease with its significant incidence of malignant degeneration. Such a study reveals that the solitary neurofibroma, the neurinoma and the neurogenic sarcoma all arise from the cells of the sheath of Schwann, that is, from the connective tissue coverings of peripheral and central nerves.

Despite this microscopic differentiation all of the malignant tumors here mentioned manifest sufficiently similar gross characteristics to warrant saying that with few exceptions they present the same common problem to the surgeon. Since they present this common problem, we feel justified in discussing them under the common heading of "encapsulated" fibrosarcoma of the soft tissues.

Most fibrosarcomas arising from soft tissues (except those of retroperitoneal and intraperitoneal origin) usually stem from subcutaneous or intermuscular fascial tissues and even though somewhat low in general incidence their gross appearance of apparent encapsulation is known to surgeons (Fig. 1). It is not uncommon to find them densely adherent to tendinous aponeuroses, this frequently seeming to be the apparent point of origin. We have noticed that these tumors frequently encompass an occasional nerve trunk of moder

ate size along with the accompanying blood vessel, but whether this could be considered as a demonstration of nerve origin is difficult to state without histological study. The fibrosarcoma and the synovioma have in our experience been single tumors sharply outlined from the surrounding tissues, growing expansively, and conforming in outline to the area in which they lie. The neurosarcoma on the other hand may be of unicentric or multicentric origin presenting the same encapsulated or circumscribed appearance. When multiple, the localized nodules arising from different parts of the same nerve may fuse with one another so that adjacent nerves running in fascia or muscle may become incorporated in the tumor process in such a manner as to give rise to a false impression of infiltration. When nerves are involved, primarily or secondarily, there is remarkable preservation of function.

There is no one characteristic gross appearance of these tumors as regards color, consistency or size since these qualities depend entirely on the relative cellular or fibrous content as well as on the presence of internal hemorrhage, necrosis or myxomatous change which in turn may be dependent upon the primary rate of growth of the tumor. Ulceration is usually a very late finding unless the tumor growth is of such unusual rapidity that it outstrips its own blood supply.

RECURRENCES

It has often been stated by way of definition that fibrosarcoma is a tumor arising from connective tissue characterized by a tendency to recur after excision. Taylor and Nathanson recently reviewed 246 cases covering a period of 25 years. Of this group 62 per cent represented recurrences when first requesting their treatment, and of the remaining 97 primary cases local control of the disease was effected in only half the patients. One feels that recurrence or persistence of the disease has become an accepted fact when discussing this type of tumor. It is this tendency toward local recurrences that has limited surgical effectiveness in the therapy of the disease. Were this controlled then an increasing number of patients would be salvaged before the well known blood borne fatal metastasis takes place.

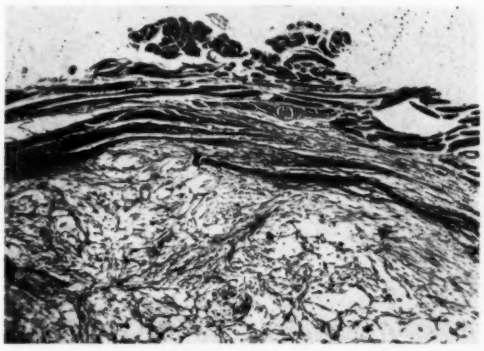


Fig. 2. Fibromyxosarcoma presenting a well defined capsule with attachment to nearby muscle due to tumor cell permeation resulting in partial destruction of the capsule.

Study has shown that in general there are four different microscopic mechanisms, any one, two, three or four of which may be instrumental in the production of the recurrence. The first, and probably most common, mechanism is that of extension of the tumor through its capsule with quite minor involvement of a nearby structure. This is far more obvious to the microscopist than to the surgeon. Although this may be overlooked in the gross specimen, it may be noted on careful examination as a point of minor adherence to nearby muscle or it may occur at the apparent point of tumor origin (Fig. 2). In general these tumors grow in the direction of least pressure, but despite this advantage to the host, the point of origin or any other point of attachment may present areas in which the tumor has penetrated the capsule, even dissolving it at times to invade the surrounding tissue with the capsule appearing grossly intact (Fig. 3). A pseudocapsule may even form to confuse the gross picture, there being a layer of fibrous tissue thrown up in front of the advancing tumor. Such permeation of tumor cells produces a focus which, if left *in situ*, will be a nidus for local recurrence.

The second mechanism pertains to the factor of lymphatic spread. This is a neglected subject because lymph node involvement typically occurs late in the course of the disease, although in 1926 Hertzler reported a patient with early involvement. It has been noted as high as 8 per cent in a series of 256 cases.

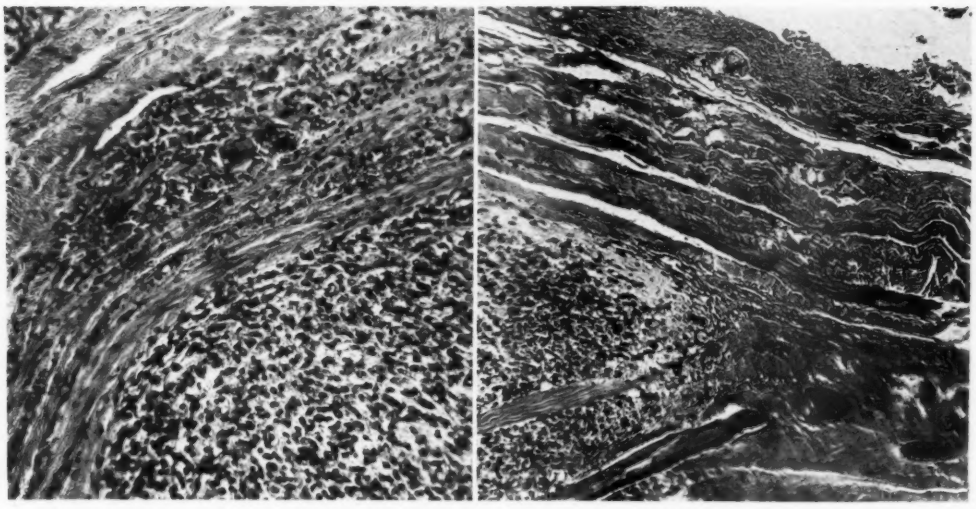


Fig. 3. a, left, Penetration of fibrosarcoma through its own capsule. b, The spread of cells at the apparent point where the tumor had its origin from the fibrous aponeurosis.

Long duration, large size of the primary tumor, local recurrence after excision and ulceration are prominent findings in proven instances of lymphatic metastasis. There is no doubt but that the tumor is slow to reach the larger lymphatic regional collecting depots, but the fact that such does occur must make one realize that involvement of lymphatic channels in the areolar tissue about the tumor at the time of excision is a potential hazard for recurrence. Under such circumstances local as well as distant spread of the tumor becomes more likely during the surgical procedure since many new tissue spaces are laid open to the tumor cells.

The third mechanism concerns the concept of multicentric origin of some of the tumors. This follows from the original observations made by Geschickter (3, 4) and by Stewart and Copeland. Working with neurogenic sarcoma they have noted the frequent development of a tumor after surgery higher up in the nerve trunk. Geschickter concluded that this represented an extension from the original tumor along the perineural lymphatic spaces. In the same manner he implicated the perivascular lymphatics of large vessels which were connected with the main tumor mass. On the other hand Stewart and Copeland have considered such a neoplasm to be an independent new growth arising in the condemned segment of the same nerve, thus attributing a certain tendency toward malignant degeneration to the nerve structures. In studying the malignant changes in 466 patients with von Recklinghausen's disease, Hosoi has shed light on the problem by stating:

"In résumé, malignant transformation takes place in about 13 per cent of all cases of von Recklinghausen's disease. When this happens, the tumor grows rapidly and tends to recur locally even after repeated operative measures.... In some cases the mere extirpation of a malignant tumor or even a benign one appears to stimulate another neurofibroma distantly located to undergo sarcomatous transformation."

The accompanying photomicrographs present an excellent example of multicentric origin of malignant neurinoma arising within the intermuscular fascial planes of the erector spinae muscle group (Fig. 4.). The differential identification here lies between a lymphatic metastatic nodule lying in the soft areolar tissue surrounding the primary encapsulated tumor and a second primary neoplasm arising in a nearby branch of the same nerve from which arose the original neurinoma. Close micro-

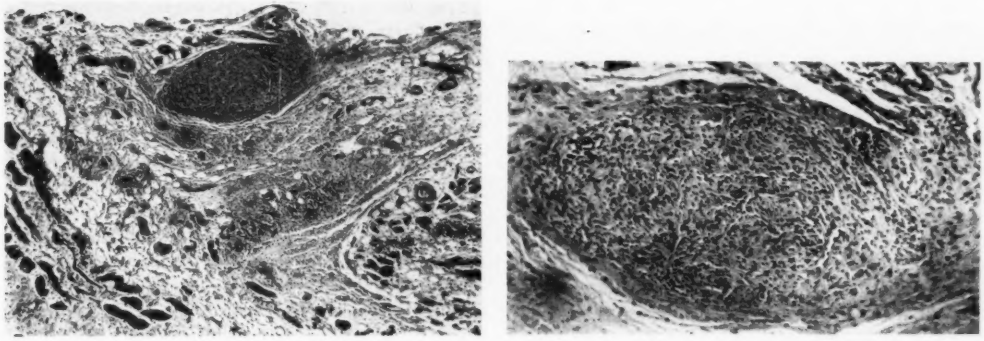


Fig. 4. a, left, Second primary malignant neurinoma found in areolar tissue surrounding an encapsulated neurinoma of the back. b, Higher magnification shows the mimicry of structure including the slight fibrous capsule. The tumor apparently did not reach within a lymphatic channel.

scopic study makes the latter opinion the more tenable.

The fourth mechanism concerns the now well substantiated phenomenon of autoinoculation or implantation at the time of surgery due to spillage of tumor cells into the wound. The experience of Harrell and Volk is cited in this regard. These men reported an accidental autogenous transplantation of an ulcerated fibrosarcoma of the heel to the left thigh during the application of a pedicle skin graft. This was explained as due either to direct extension of the tumor through the graft or by accidental contamination of the incision at the donor site with tumor cells. The experience of Greene in successfully transplanting human fibrosarcoma to the anterior chamber of the eyes of guinea pigs and carrying it by serial transfer through 14 generations adds further weight to this concept.

TREATMENT

Before considering the application of these observations as they might be related to therapy, it is of interest first to note the report of Meyerding, Broders and Hargrave covering a 20 year span in which they recorded a 3 year survival rate of 21 per cent in 132 patients afflicted with fibrosarcoma. Since it is now generally agreed that radiation therapy is of little value (1, 12), the obvious conclusion to be drawn from such a pessimistic report as well as our own experience is that the primary surgical attack on these tumors appears to be inadequate in many instances. For these tumors located in the extremities, one might easily conclude that the percentage of cures could be increased by routine amputation but closer examination of a large series of cases reveals that this would result in an unnecessarily large number of amputees without materially lowering the death rate. Thus Meyerding and his co-workers reported that of 28 cured patients in their series only 6 had amputations performed. There is no doubt but that amputation is absolutely mandatory when complete excision is impossible, when deep nerves or vascular trunks appear to be involved, or when recurrence has taken place for the first or second time. Even in this last mentioned group, where recurrence has taken place, Meyerding reports but five cures in 34 instances where amputation was performed in the absence of demonstrable metastases. We realize that proper evaluation of available statistics on amputation for these tumors is difficult because of the previous inaccurate histological differentiation and also since this maneuver usually has been reserved for the advanced cases, but nevertheless the procedure does not seem to fit all the requirements for the patient requesting primary care.

The answer to this low rate of cure seems to lie in the performance of a more complete local excision at the time of the first surgery. In a negative way this means that the tumor should not merely be "shelled out" of its connective tissue bed. In a positive way this

means that the tumor and its areolar tissue bed plus any attached muscle, nerve, or blood vessel should be excised *en masse*. Blunt dissection here is not the answer. In reviewing the operative reports concerning the removal of some of these tumors, we have noted that the tumor frequently was shelled from its bed down to an apparent point of origin or at least to a point of attachment from which it was cut free with a scalpel. Because of the lymph drainage within a muscle, it is felt that partial excision of muscle may be inadequate when a muscle belly appears to be invaded. In such instances our experience would lead us to suggest that complete extirpation of the muscle or group of muscles is far superior to a recurrence. Section of nerve trunks and ligation of vascular highways should best be performed as far as possible from the tumor. If involvement of these structures presents insufficient indication for amputation, then the least we can advise is wide excision and restoration of nerve continuity with fresh autogenous or homogenous grafts. The logic of such a procedure has been clearly demonstrated (2). With the more prevalent ability in skin grafting there seems to be no excuse for allowing any possibility of recurrence by cutting too close to the tumor when excising overlying skin.

APPLICATION OF SURGICAL EXCISION

From the practical standpoint these generalities, if accepted, must be reduced to terms of procedure for the individual patient. In other words some consideration must be made concerning the incision to be used as well as the part to be played by the pathologist if needed in establishing the diagnosis. These steps must be carried out with sufficient ease and safety to allow for the most efficient surgical extirpation possible. Our feeling at this time is that most tumors found in the areas mentioned eventually are proved to be malignant following microscopic study. Very few instances of purely benign tumors can be found among such a group except for the fibromas with their characteristically long history and small size, and the lipoma which is quite easily identified. Wilson found that 90 per cent of 111 specimens of fibrosarcoma measured over 5 centimeters in greatest diameter while the same percentage of fibromas measured under 3 centimeters. Such information may be helpful but not unless correlated with duration and rate of growth. Certainly any small subcutaneous nodule which has persisted for years and which suddenly begins to grow rather rapidly will be suspected of malignant change before it reaches the critical size of 5 centimeters.

If the diagnosis is obvious a more vigorous attack can be planned at the earliest phase of the surgical intervention. There is no doubt but that the element of surgical judgment is prominent in such a matter and for the sake of clarity it is logical to liken this problem to that of breast carcinoma. In many instances the experienced surgeon can with the fullest justification proceed with his radical mastectomy without the aid of a frozen section because to him the pathological diagnosis is quite evident while in other instances he will rely upon the microscope following a local excision before going on with the more radical procedure. Unfortunately the pathologist finds himself at a disadvantage with the frozen section technique when attempting to diagnose some of these tumors without the use of special stains. Theoretically this very practical procedure loses some of its utility but this does not mean that it should be omitted from our armamentarium when we are in doubt, for it can establish in a general way the degree of malignancy that an individual tumor may possess. By this we mean that a "mad dog" type of tumor can be differentiated from a "sleeping dog" type irrespective of the cellular origin. The relative proportion of cells to fibrillar intercellular substance is probably the best single criterion for estimating the degree of malignancy in these tumors.

SUMMARY

The high mortality rate in patients afflicted with fibrosarcoma presents a severe challenge to the surgeon. Some of these patients probably never will be cured but many can be salvaged by preventing fatal blood-borne metastasis. This form of metastasis appears to be related to the incidence of local recurrence more than to the incidence of the disease. The local extirpation of the disease thus becomes

of paramount importance. Since the tumor frequently occurs in the extremities the question of amputation also must be considered among the methods of obtaining local control of the disease. At the present time we feel reluctant to advise amputation when a satisfactory local excision can be first achieved, but on the other hand if a careful evaluation of the speed of growth, the size, location and histological nature of the tumor would warrant it, amputation should be carried out as the procedure of choice. If the tumor presents as a recurrence, it is highly likely that a high amputation should immediately be advised unless a more adequately wide excision could still be performed. In such instances, the size of the resulting defect should not be a barrier for adequate excision as long as proper skin replacement can be achieved. It is not possible to outline typical procedures to be followed for each instance but we are impressed with the fact that the successful outcome in most instances will be determined by the procedure used at the time of the first surgical intervention.

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PANCREATIC REFLUX DELIBERATELY PRODUCED

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THE importance of biliary-pancreatic reflux as an etiological factor in the production of acute pancreatitis or acute cholecystitis has been amply demonstrated in recent years (1, 3, 5, 7, 8, 9).

In the past, pancreatic reflux was demonstrated in about 25 per cent of patients in whom a tube was placed in the biliary tract at operation (2, 6). The diagnosis was based on two methods: (1) the finding of pancreatic enzymes (notably amylase) in high concentration in the bile recovered from the tube drainage and (2) the visualization of the pancreatic duct when iodized oil was injected into the tube draining the biliary tract.

These observations frequently depended on a fortuitous conjunction of events. As a rule, pancreatic enzymes could be found in the biliary drainage only occasionally, usually after meals (2), but sometimes only in samples obtained late at night (Table I). Similarly, the pancreatic duct could be visualized during the performance of a cholangiogram only during such accidental periods when the pancreas was not secreting and when in addition the sphinc-

From the Department of Surgery, New York University College of Medicine.

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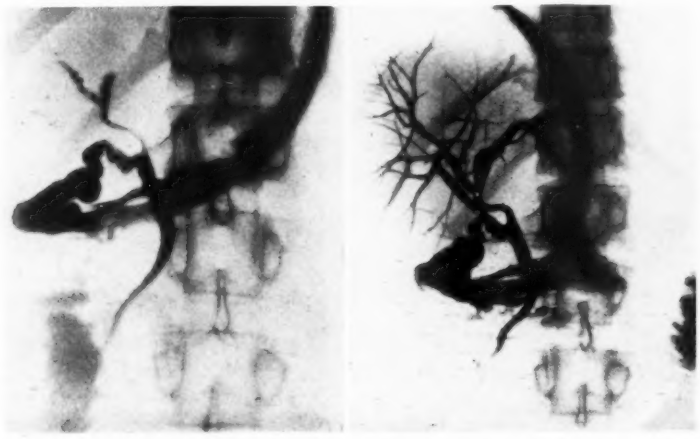
TABLE I.—AMYLASE CONCENTRATION (MGM. PER 100 C.C. GLUCOSE) IN T-TUBE DRAINAGE BILE OBTAINED AT 2 HR. INTERVALS FOR 24 HRS.

Time of bile collection at 2 hr. interval	Days after operation	
	42	45
Noon	0	0
2:00 p.m.	0	0
4:00 p.m.	0	0
6:00 p.m.	0	0
8:00 p.m.	0	0
10:00 p.m.	0	258
Midnight	0	90
2:00 a.m.	0	66
4:00 a.m.	0	0
6:00 a.m.	888	600
8:00 a.m.	920	832
10:00 a.m.	0	0



Figs. 1 and 2. Before the administration of morphine (Fig. 1, left), the injection of iodized oil fills out the common duct, then runs into the duodenum. Only the terminal parts of the hepatic duct are outlined. Two minutes after subcutaneous administration of morphine, the continued injection of iodized oil results in the visualization of the whole biliary tract. This is due to the increased resistance of the sphincter of Oddi.

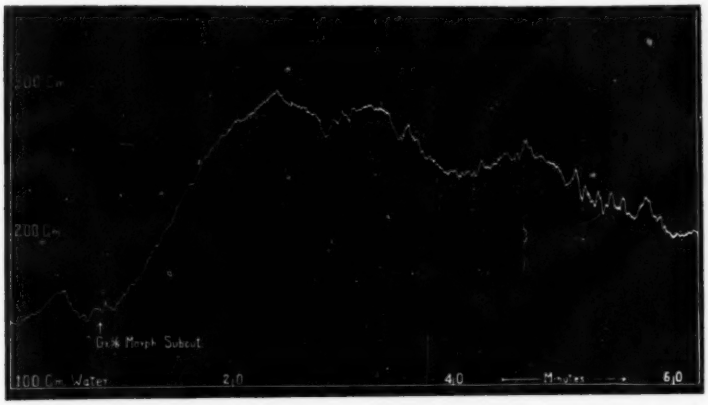


Fig. 3. Kymographic tracing of the resistance of the human sphincter of Oddi. Following the administration of morphine, 1/6 grain, the normal resistance of the sphincter (150 mm. of water) rises to 300 millimeters and gradually subsides to 200 millimeters in one hour.

ter of Oddi was sufficiently spastic to permit the reflux of iodized oil.

An effort, therefore, was made to determine the optimum conditions under which reflux of pancreatic juice could be routinely obtained and the pancreatic duct could be visualized most frequently during cholangiographic studies.

When the resistance of the sphincter of Oddi is normal (about 150 mm. of water) iodized oil passes through the common bile duct into the duodenum without filling the fine bile ducts (Fig. 1). Two minutes after the subcutaneous injection of 1/6 grain of morphine (Fig. 2), the whole biliary tract can be visualized. Kymographic tracings (Fig. 3) reveal these pressure changes clearly (4). One can note, however, that the resistance of the sphincter which rises to 300 mm. of water comes down to 200 mm. at the end of an hour. The intraduodenal injection of hydrochloric acid causes a temporary spasm of the sphincter lasting 10 minutes (Fig. 4). When the sphincter is moderately spastic (Fig. 5) in cases in which the bile and pancreatic ducts join above the sphincter, the iodized oil runs up the main pancreatic duct and out through the accessory pancreatic duct (Santorini), when this duct is present. In the

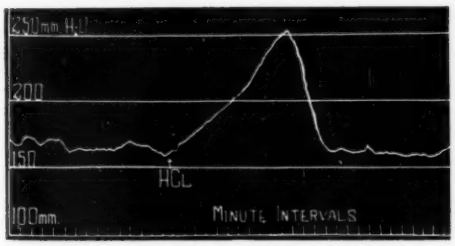


Fig. 4. The intraduodenal installation of tenth normal hydrochloric acid causes immediate spasm of the sphincter of Oddi. The resistance rises from about 150 to 250 millimeters of water and the effect wears off in about 10 minutes.

Fig. 5. Visualization of the main (Wirsung) and accessory (Santorini) pancreatic ducts. The iodized oil passes down the common bile duct, meets with resistance from the sphincter of Oddi, and passes up the main pancreatic duct of Wirsung and then through the accessory duct of Santorini into the duodenum.

Figs. 6 and 7. Injection of iodized oil shows considerable spasm of the sphincter of Oddi (Fig. 6, left) since the hepatic ducts are outlined to a considerable extent before the oil passes into the duodenum. At the same time, a portion of the pancreatic duct (arrow) is filled. The junction of the common and pancreatic ducts at the ampulla of Vater is clearly visualized. Following the administration of morphine (Fig. 7) the whole biliary tract is outlined. The increased tonicity of the duodenal wall as a result of morphine action causes compression of the intramural portion of both the common and pancreatic ducts. The ampullary junction of these ducts are, however, still clearly outlined (arrow).

following case (Fig. 6) one can clearly see the submucosal junction of the two ducts. Two minutes after the injection of morphine (Fig. 7) the whole biliary tract is outlined due to spasm not only of the sphincter, but of the duodenal wall through which both ducts pass.

When the bile and pancreatic ducts are connected by a fully unobstructed passageway as in the following unusual case (Figs. 8 and 9) which Dr. Ralph Colp of The Mt. Sinai Hospital kindly allowed me to study, passage of pancreatic juice into the biliary drainage was

Figs. 8 and 9. Injection of iodized oil reveals a hugely dilated choledochus and markedly dilated tortuous pancreatic duct (Fig. 8). The narrow submucosal junction of the two ducts is clearly seen (arrow). Another view (Fig. 9) outlines the whole dilated pancreatic duct as far as the tail.

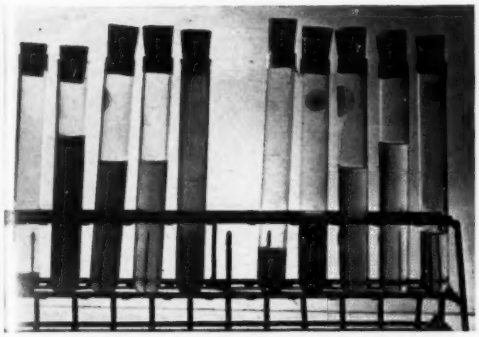


Fig. 10. Simultaneous collection of T tube bile drainage (5 tubes on left) and duodenal drainage (5 tubes on right) following the injection of secretin in the case illustrated in Figures 8 and 9. The first tube contains drainage of the 10 minute control period, and the following consecutive tubes drainage of 10, 20, 40, and 60 minutes after secretin stimulation. Note the variations in the density especially of the T tube drainage, due to spurts of almost water clear pancreatic juice mixing with the bile.

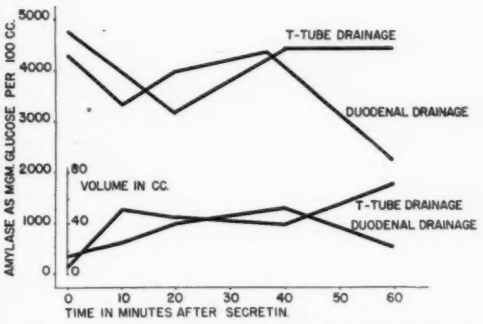
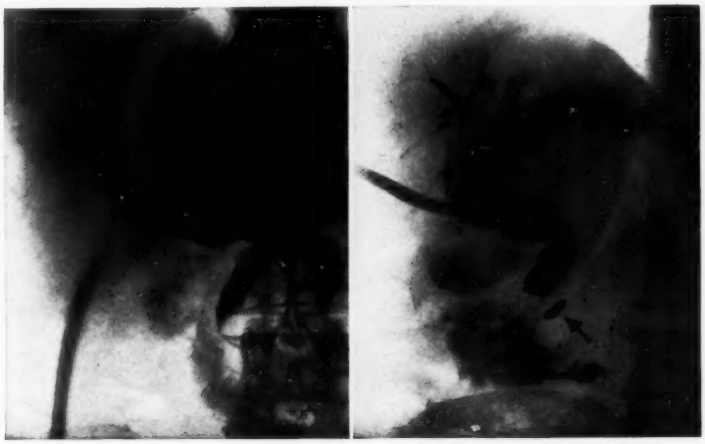


Fig. 11. Concentration of amylase in T tube and duodenal drainage following the intravenous injection of secretin in the case illustrated in Figures 8, 9, and 10. The variations in the amylase content of the two drainage fluids appear to be related to the changes in the volume of secretion.

of quite frequent occurrence. When secretin was administered intravenously to produce pancreatic reflux under controlled basal conditions, it was found (Fig. 10) that about half the pancreatic juice passed into the duodenum while the other half passed up the common bile duct. Gushes of almost water clear bile (containing pancreatic juice) would alternate with darker bile coming unmixed from the liver. Similarly the duodenal drainage contained occasional traces of bile but frequently was water clear. The composite result depended on the resistance of the sphincter and the volume of secretion at various intervals.

When this drainage material was examined for amylase (Fig. 11), it was seen that the concentration of amylase was approximately equal in the biliary and the duodenal drainage, the



Figs. 12 and 13. Injection of iodized oil in this case in which amylase was recovered in the T tube drainage, revealed a moderately spastic sphincter and a dilated common bile duct (Fig. 12, left). The pancreatic duct (arrow) was visualized following the injection of morphine, only after two previous failures (Fig. 13).

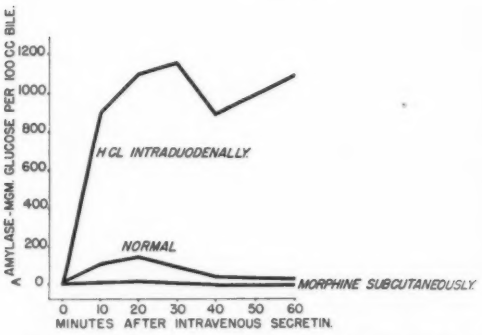


Fig. 14. The optimum conditions for the production of pancreatic reflux. In this case (Table I and Figs. 12 and 13), the injection of secretin was followed by the appearance of amylase in low concentration in the 10 and 20 minute samples only. Morphine stopped all reflux due to spasm of sphincter of Oddi and duodenal wall. Hydrochloric acid intraduodenally produced spasm only of the sphincter and resulted in a maximum reflux of pancreatic juice.

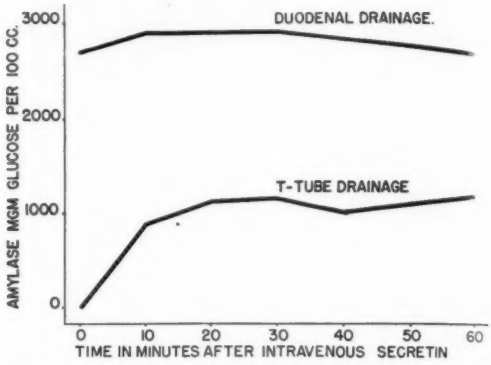
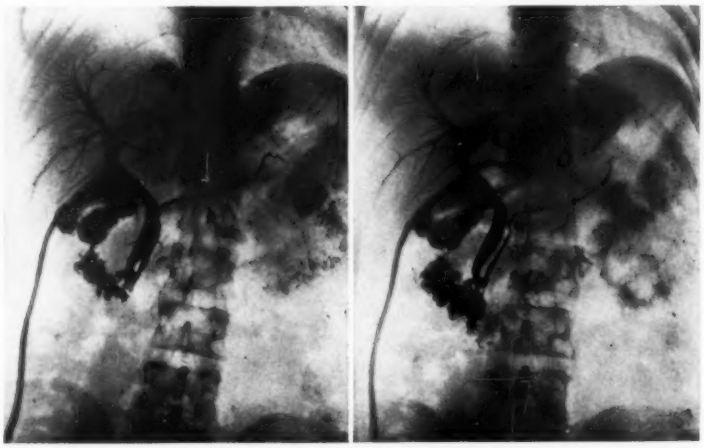


Fig. 15. The relative concentrations of amylase in the T tube drainage and in the duodenal drainage following spasm of the sphincter of Oddi produced by intraduodenal administration of hydrochloric acid (see Fig. 14). This indicates that about one-third of the biliary drainage consisted of pancreatic juice.

small differences being due to variable admixtures of bile.

However, in most cases of pancreatic reflux, amylase was found in the biliary drainage quite infrequently and the pancreatic duct was visualized only after producing spasm of the sphincter of Oddi by means of morphine. In the following case (Figs. 12 and 13) the pancreatic duct was visualized by injection of iodized oil only after the third attempt, and amylase was found in the bile after six samples of bile were analyzed.

Accordingly the patient was given intravenously a standard dose (80 clinical units) of



Figs. 16 and 17. The optimum conditions for visualization of the pancreatic duct. Iodized oil was injected into the biliary tract in a patient who had been fasted, had all stomach contents aspirated by Levine tube suction for 2 hours previously, and had received a subcutaneous injection of 1/6 grain morphine 1 hour previously—note complete filling of pancreatic duct (arrow). Slight rotation of the patient (Fig. 17, right) clearly reveals the anatomical relationship of the two ducts and their junction above the sphincter of Oddi.

secretin and the biliary drainage collected at 10, 20, 40, and 60 minute intervals (Fig. 14). Amylase was recovered only in the 10 and 20 minute samples. When morphine was given just before the injection of secretin, no amylase was recovered due to the fact that the spasm produced by the morphine involved not only the sphincter of Oddi but also the duodenal wall, shutting off any reflux. In a third procedure, a duodenal tube was passed and following the injection of secretin intravenously, 20 cubic centimeters of one-tenth normal hydrochloric acid was introduced intraduodenally every 10 minutes. This produced spasm of the sphincter but not of the duodenal wall, and as can be seen, a large amount of pancreatic juice (as represented by amylase) was recovered in the biliary drainage. The concentration of amylase recovered in the bile as compared to the concentration in the duodenal contents (Fig. 15) showed that one-third of the biliary drainage consisted of pancreatic juice. There can be no question that such procedures which control both the flow of pancreatic juice and the resistance of the sphincter of Oddi will result in the discovery of the maximum incidence of pancreatic reflux.

Similar principles were applied in the visualization of the pancreatic duct by iodized oil. Since two main factors, food and hydrochloric acid, stimulate the secretion of pancreatic juice, the patient was fasted and a Levine tube was passed 2 hours prior to x-ray examination, for continuous suction of the stomach contents. To control the resistance of the sphincter of Oddi, morphine, 1/6 grain, was given one hour prior to the cholangiographic study. As the kymographic tracing in Figure 3 demonstrates, 1 hour after morphine injection the resistance of the sphincter falls almost invariably to about 200 millimeters of water. By this time, the spastic effect of morphine on the duodenum has worn off. When iodized oil was injected into the common bile duct under such conditions, the whole pancreatic duct was visualized (Figs. 16 and 17).

CONCLUSION

Therefore, it can be seen that control of pancreatic secretion and control of the resistance of the sphincter of Oddi by various means can be utilized to diagnose pancreatic reflux after operation on the biliary tract. Similar methods are being developed now to diagnose this condition on the operating table.

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THE EFFECT OF EARLY POSTOPERATIVE RISING ON THE RECURRENCE RATE OF HERNIA

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THE original article on this subject was written by Ries, a gynecologist in Chicago in 1899. He was impressed by the rapid return of strength in the patients who rose early after operation and he noted the lack of unfavorable complications resulting from early rising. Although the practice of early postoperative rising was taken up by many of the European surgeons, it was not widely used in this country until interest in the subject was stimulated by Leithauser of Detroit in 1941 when he published a series of 436 cases. Since the publication of Leithauser's first article, there have appeared a number of clinical reports on early postoperative ambulation.

In June of 1942 a critical investigation of early postoperative rising was undertaken at the Peter Bent Brigham Hospital (1). This was to study what effect early ambulation has on postoperative complications, and whether it has any effect on the late operative results. Since postoperative complications are most common among patients having major intra-abdominal surgery, this group was used to test the effect of early postoperative rising on postoperative complications. Two hundred and thirty-eight such patients who had risen on the first or second postoperative day were compared with 443 patients who got up after the seventh postoperative day. Our pertinent conclusions of that study were that the incidence of atelectasis was slightly lower in the early-rising group (4.6% compared with 6.3%), and that the incidence of deep-leg-vein thrombophlebitis, however, was slightly higher in the early-rising group (2.9% compared with 1.8%). With respect to the incidence of postoperative wound disruption, there was a slight reduction in the early-rising group (1.3% against 2.7%).

From the Peter Bent Brigham Hospital, Surgical Service.
Presented in the forum on Fundamental Surgical Problems before The Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–30, 1946.

Today we present the results of a controlled study to determine the influence of early postoperative rising on the recurrence rate of hernia. The control group consists of 202 various herniorrhaphies on 177 patients. These patients got out of bed on the seventh to the fifteenth postoperative day. They were followed from 6 months to 7 years. The test group consists of 174 herniorrhaphies in 159 patients. The majority of the test group rose on, or before, the first postoperative day; 12 patients rose on the second day. They were all followed from 6 months to 4 years. Interrupted, fine silk technique was used in all cases of both groups.

The technique of getting the patient out of bed is essentially the same as Leithauser's. On the morning following operation, the patient is turned on the side operated upon. He flexes his hips and knees so that his lower legs are at the edge of the bed. The nurse locks her elbow in the patient's elbow, and the patient pushes his feet off the side of the bed as the nurse assists him up sideways to a sitting position. As the patient sits on the side of the bed, slippers with heels, or shoes, are put on before he stands on the foot stool. While standing, he is encouraged to breath deeply and to cough several times. The patient then walks around the bed and sits in his chair for about 20 minutes. As he returns to bed, the walking and coughing are repeated. He is assisted out of bed in this manner twice daily until he can get up himself which in cases of herniorrhaphy is usually on, or before, the third postoperative day. If the patient wishes to get out of bed on the day of the operation, he is allowed to do so, unless there is some specific contraindication. Many of the patients who had had herniorrhaphy performed under local, nerve-block anesthesia, got out of bed to eat lunch on the day of operation.

There was no selection among the patients who rose early following herniorrhaphy. The

TABLE I.—THE RECURRENCE RATE OF INDIRECT INGUINAL HERNIAE

Type of operation	Non-early risers		Early risers	
	Number	Recurrence	Number	Recurrence
Halsted	37	2	30	3
Bassini	85	2	72	2
Other	Ferguson 5 McVay 2 Other 2	0 0 1	Ferguson 2 McVay 5 Orchidectomy 3 Others 2	0 0 0 0
Totals	131	5 (3.8%)	114	5 (4.3%)

TABLE II.—THE RECURRENCE RATE OF DIRECT INGUINAL HERNIAE

Type of operation	Nonearly risers		Early risers	
	Number	Recurrence	Number	Recurrence
Halsted	27	5	22	4
Bassini	18	0	10	0
Others	McVay 2 Gallie 2	0 1	McVay 3 Orchidectomy 1	0
Totals	49	6 (12.2%)	36	4 (11.1%)

group includes older patients, patients with poor abdominal wall structures, and patients who had all types of anesthesia and operative repairs.

As a group, the early risers were somewhat older because the younger patients were in the Army during the period when most of the early-rising patients were operated upon. As we review the two groups, we are again impressed by the rapid postoperative recovery which is found to be present among the group of early-rising patients.

In comparing the recurrence rates in the two groups, the results are classified with respect to the method of operative repair[1] and the type of hernia, that is, indirect, direct, femoral incisional, and umbilical. Indirect inguinal hernia according to Watson's monograph, carries a recurrence rate of 5 to 10 per cent. Shelley in an exhaustive study of over 1600 indirect inguinal herniae at the New York St. Luke's Hospital found a recurrence rate of 7.2 per cent.

[1]The Halsted repair refers to Halsted's modified repair in which both the conjoined tendon and the external oblique fascia are sutured below the spermatic cord so that the cord is transplanted into the subcutaneous tissue and the external ring approximates the internal ring in position.

TABLE III.—THE RECURRENCES IN FEMORAL, INCISIONAL, AND UMBILICAL HERNIAE

Type of hernia	Nonearly risers		Early risers	
	Number	Recurrence	Number	Recurrence
Femoral	8	2	6	1
Incisional	10	0	11	0
Umbilical	3	0	7	0

TABLE IV.—TOTAL RECURRENCE RATE OF INGUINAL HERNIAE

Type of hernia	Nonearly risers			Early risers		
	Number	Recurrence	Per cent	Number	Recurrence	Per cent
Indirect	131	5	3.8	114	5	4.3
Direct	49	6	12.2	36	4	11.1
Totals	180	11	6.1	150	9	6

Table I gives a tabulation of the recurrences in indirect inguinal herniae. It shows that, in the nonearly-rising group, there were 5 recurrences in 131 operations and that in the early-rising group, there were 5 recurrences in 114 operations. This is a recurrence rate of 3.8 per cent in the nonearly risers and 4.3 per cent in the early risers.

For direct hernia, Watson gives the recurrence rate as between 10 and 20 per cent. It may even be higher. As recently as 1942 Page reported a recurrence rate for direct hernia of 35 per cent.

Table II presents a tabulation of the recurrences for direct inguinal herniae which shows that, in the nonearly-rising group, there were 6 recurrences in 49 repairs. In the early-rising group there were 4 recurrences among 36 repairs. This is a recurrence rate of 12.2 per cent in the nonearly risers and 11.1 per cent in the early risers.

The recurrences in the few femoral, incisional, and umbilical herniae are listed in Table III. This shows no appreciable increase in recurrences in this small group as a result of early rising.

Table IV gives the total recurrence rate in inguinal hernia. It is seen that the recurrence rate in 180 inguinal herniorrhaphies treated

by postoperative bed rest is 6.1 per cent, whereas, the recurrence rate in 150 inguinal herniorrhaphies treated by early rising is 6.0 per cent.

CONCLUSION

We conclude from these data, that early postoperative rising exerts no significant effect on the recurrence rate of hernia.

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THE USE OF THE MALE SEX HORMONE IN WOMEN WITH BREAST CANCER

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WE have now arrived at the point where it has become profitable to pursue the use of hormone therapy in certain types of human cancer. Huggins made one of the most important contributions that have been made in many years in the field of cancer, when he was able to produce 25 per cent cures in prostatic cancer—a disease widely recognized to have an extremely high mortality. His study of the hormone influence in this disease naturally suggested exploration of other fields where cancer is either produced or materially influenced by the sex hormones. Beside the prostate it is patent that other organs such as the breast, uterus, ovaries, adrenal, testes and thyroid should each receive serious attention and experimentation.

I recently made a study of 5000 cases of early breast cancer relative to their ages, at the time of the development of their cancer.

The peak of the greatest number developing cancer, was 45 years. This age probably represents the time when certain chemical changes are present deviating somewhat from the normal ovarian hormone. The ovaries are undergoing at this age, certain changes leading up to the menopause which comes on at an average of 46½ years.

On the other hand, the year when next to the greatest number develop breast cancer, is age 60 years; and here we probably have a patient who has practically no ovarian hormone output. It is possible that the 13 or 14 years since having a definite ovarian function, as evidenced by menstruation may represent a complete lack of ovarian hormone output; and may represent a possible cause for the production of breast cancer, in the older age group. This theory fits well into the fact that the women of 60 years and older with breast cancer, are improved by the use of the estrogens.

During the past several years my department has been making a clinical experimental study on approximately 200 cases of cancer of the female breast in which testosterone propionate has been employed.

In the beginning the results of this therapy *when using small amounts* seemed to be of no value (Farrow and Woodward). I next treated 48 patients in my private practice employing a daily dose of 25 milligrams intramuscularly to each patient (175 mgm. weekly). It soon became obvious that in certain cases of advanced breast cancer, and more particularly in those metastatic to bone, that we were dealing with a very potent agent capable of producing striking clinical improvements as well as changes some of which were demonstrable by x-ray films.

Up to this time we had been hampered in our clinical research by the high cost of testosterone propionate; and at this juncture Dr. Henderson of the Schering Corporation generously made it possible for us to commence our new attack employing large doses.

Dr. Julian Herrmann and I then began by giving some patients as much as 100 milligrams daily by intramuscular injections of the agent in oil. We varied the dose using in some instances the testosterone pellets, placed subcutaneously in order to obtain a more prolonged absorption of the agent. After much trial and error we arrived at our present dose of 100 milligrams by intramuscular injection three times weekly for a period of 8 to 10 weeks, making a total dosage of 2400 to 3000 milligrams. We freely admit that we have not come to a final conclusion as to what should be the exact dose; how much total should be delivered; and how long it should be continued. Obviously many of these factors must be determined and will be influenced by whether or not the patient

The studies were made possible by a grant from Mr. Louis Marx to the Breast Service of the Memorial Hospital, New York.

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still menstruates, on whether or not her ovaries have been made functionless by x-ray or surgical castration, as well as many other factors.

At the present time the work is being pursued by my associates and myself not only in the advanced cases, but also in the new cases of early operable breast cancer.

It has now gotten almost beyond the point where it is necessary to demonstrate the value of testosterone therapy by giving case reports, as we have already placed ample cases in the literature which show the value. We are now at the point where we can draw general conclusions of what may be anticipated by this therapy.

Our experience has shown that in only a small percentage of cases is improvement to be anticipated when the cancer involves the soft tissues such as liver, lungs, brain and local skin recurrence. It is true that in a few instances, there have been striking improvements where an advanced ulcerating breast cancer with surrounding skin nodules, axillary nodes and neck nodes were involved; where masses were metastatic to the lungs; and in one instance where the patient was having convulsions from metastatic disease in the brain. However, I fear it must at present be taken for granted that most such cases receive no benefit aside from the temporary general improvement which frequently comes as a result of testosterone injections.

On the other hand, a most striking improvement is obtained in most of those cases having bone metastasis. There is some specificity or predilection for the agent to do its work of repair in the bone cases—and as yet we do not understand the reason. It is probable in the metabolism of bone repair under the influence of testosterone, that the billions of cancer cells are "snowed under" by the copious deposit of calcium precipitates especially in areas of bone destruction—a locking-in process where cell reproduction is difficult. Similar to prostate cases, the cancer cells will still be present after testosterone therapy. We do not yet know whether the improvement of the bone destruction by the invading cancer is confined to cases of breast cancer alone, or whether metastasis to bone from some other type of cancer may also be improved by testosterone such as from thyroid or ovaries. It is important that this study be pursued and that a study in cases of primary bone sarcoma also be carried out.

After approximately 2 weeks of testosterone therapy, the relief of pain, from bone metastasis is usually very real. Lack of sleep due to pain is replaced by a natural sleep. It is usually possible to cease giving narcotics which may have been given in large amounts. Some of our patients who had such pain that it was not possible to continue their work, were able to return to their jobs in comfort by the end of a month of therapy. The areas of bone destruction as evidenced by absorption of the calcium salts, by collapse of vertebrae, and by fracture of ribs, are filled in with dense callus similar to that seen following x-ray therapy. How long this improvement in the osseous tissue persists is not yet known. However, we have 3 cases in which disease was confined to bone, having no ascertainable soft tissue involvement, living free of evidence of disease or symptoms for a period of 1½ to 2 years after commencing the testosterone therapy.

A brief example of one of these cases was a woman aged 71 years who had been confined to her bed for a period of 10 months, with widespread bony metastases to the spine, pelvis, and ribs several of the latter being fractured. After 4 weeks of testosterone therapy, she was able to leave her bed. At the end of 3 weeks of therapy she developed as is so common, the feeling of elation and well being. By the end of 6 weeks she "was walking all over the city," free from symptoms. The only symptom which bothered her was the annoyance and the irritation of the enlarged clitoris. This patient started on her testosterone therapy in July, 1944, and up until December 1, 1946, a period of 2 years 4 months, was living in good health. Three weeks ago she began to have nausea which has persisted, and it may be suspected although not demonstrable, that she may have metastases to the liver or to the abdominal lymph nodes. It is not unusual for a patient with metastasis to bone, to keep the disease confined there for some time, before finally spilling over into soft tissues such as the lungs or abdomen.

Fig. 1. Demonstrating destruction of a large area of frontal bone by metastatic cancer from breast.

Fig. 2. The same patient 10 weeks later following 24 injections, 100 milligrams each, of testosterone propionate, totaling 2400 milligrams. The area of destruction has been filled in by callus and the mass protruding from the forehead has disappeared.

In cases of widespread bony metastasis the use of testosterone propionate seems more efficacious, longer lasting, and more practical than x-ray therapy. When it becomes necessary to treat multiple widespread areas of metastatic bone disease, with the x-rays, it becomes a matter of great difficulty to deliver so many doses over so many areas, not only because of the nausea which frequently accompanies such treatments; but there is also the practical problem of bringing a patient who suffers intensely from bone metastasis to the hospital or x-ray laboratory; furthermore such a large number of x-ray treatments, may produce an anemia, in the face of which x-ray therapy itself becomes ineffective.

We have had many instances in which the skin of the patient had been so damaged by x-ray therapy that it was not possible or practical to deliver further x-ray treatments to the bones. Fortunately it is usually possible in such a case to commence with the testosterone therapy and still obtain some degree of clinical improvement.

In the advanced cases of bone metastasis the blood chemistry is fairly consistent. As a rule such a patient has a blood calcium well above the normal of 10 to 12 milligrams per 100 cubic centimeters. The blood calcium at times goes up as high as 17 milligrams. Under testosterone propionate therapy, the rule is that the blood calcium slowly comes back into normal limits theoretically being redeposited in the areas of bone destruction.

The alkaline phosphatase also acts characteristically; it is an enzyme necessary for bone repair. The normal limits are 3 to 5 milligrams. During bone repair under testosterone, this figure at times reaches as high as 15 milligrams indicating that bone repair is taking place.

Most of our work to date has been on advanced breast cancer cases. However, we have recently started to work on the early operable cases of breast cancer using the radical mastectomy supplemented by large doses of testosterone implanted into the latissimus

dorsi muscle or into the subcutaneous tissues near the wound at the time of the operation. Although we have used this combination in 135 such cases to date, we have nothing to report as yet. Two months after the operation we will again implant further doses of testosterone, on the theory that possibly recurrence and metastasis may be influenced or lessened by subjecting any remaining cancer tissue, to the unhealthy environment of testosterone bearing blood and serum. It is obvious that such a human experiment should be undertaken and evaluated.

It may be of some interest to note that in two pregnant patients with breast cancer receiving testosterone, that repeated Aschheim-Zondek tests were negative up to 5 months of pregnancy, when the patients could feel life.

It is scarcely necessary to state that the patient receiving testosterone therapy develops unpleasant masculinizing sequelae as evidenced by a deeper husky voice, hair on the face, pimples on the face and body and an enlarged clitoris which in certain cases becomes a source of great annoyance.

On the other hand, under testosterone therapy there is usually, at least temporarily, a gain in weight, a feeling of well being, a loss of bone pain, and a repair of the bone destruction caused by the metastatic disease.

As a rule the *clinical* improvements by the use of testosterone, are far more striking than the x-ray improvements reveal.

Testosterone may be employed on female patients with breast cancer at any age, while the estrogen therapy must be strictly confined to patients of 60 years and older.

It must be here emphasized that we are not stating that testosterone is a cure for breast cancer; however its effects are very profound and gratifying; but indicate that much more clinical research must be carried out in this field before we can fully evaluate dosage or final results.

RESECTION OF INTRA-ABDOMINAL CANCER THAT HAS INVADED THE ANTERIOR ABDOMINAL WALL

ALEXANDER BRUNSCHWIG, M.D., F.A.C.S., Chicago, Illinois

INVASION of the anterior wall by carcinomas primary in the abdominal viscera or invasion of the anterior abdominal wall by metastases from such growths does not constitute a situation in which radical surgical excision is necessarily contraindicated. The primary growth together with its parietal extensions may be excised *en masse* to removal, in some instances, of all macroscopic evidence of tumor. Such procedures were carried out in a limited group of patients; the histories are briefly as follows:

CASE 1. J. C., no. 283119, male, aged 66 years, was subjected to a right hemicolectomy, resection of the lower half of the stomach and elliptical portion of the abdominal wall about the umbilicus to remove a large carcinoma of the transverse colon, which was spreading to the adjacent structures mentioned. Patient is living and well, 4 years and 5 months after operation.

CASE 2. G. P., no. 332661, male, aged 63 years, had a resection *en masse* of 16 centimeters of sigmoid colon, an elliptical segment of the parietal peritoneum and deep fascia in the left lower quadrant and segment of the lower jejunum 10 centimeters in length, for carcinoma of the sigmoid which was infiltrating the jejunum and anterior abdominal wall. End-to-end enterostomy and double-barrel colostomy were performed, and the latter was subsequently closed. Patient is living and well, 2 years 5 months after operation.

CASE 3. Jaw, no. 274690, female, aged 34 years. Laparotomy was performed for removal of many peritoneal metastases from a pseudomucinous cyst—adenocarcinoma of the right ovary in 1941. A second laparotomy was done for resection of numerous metastases over the peritoneal surfaces of bowels and in the mesentery of the small intestines. A half-fist size mass infiltrating the abdominal wall in the right lower quadrant was excised together with portions of the rectus muscle. Patient is living and well 2 years 2 months after second operation.

CASE 4. J. L., no. 322684, male, aged 39 years. Resection of the abdominal wall of the left upper quadrant and subjacent recurrent colon for carcinoma, with descending colon, spleen, containing 4 metastases, and tail of pancreas. Double-barrel colostomy was done and was later subsequently closed. Patient is living 1 year 2 months after operation. He has an enlarged nodular liver due to metastases.

CASE 5. P. W., no. 379472, male, aged 58 years. A right hemicolectomy was done and 20 centimeters of

From the Department of Surgery, University of Chicago. These studies were aided by the Chas. H. and Mary F. S. Worcester Fund, University of Chicago.

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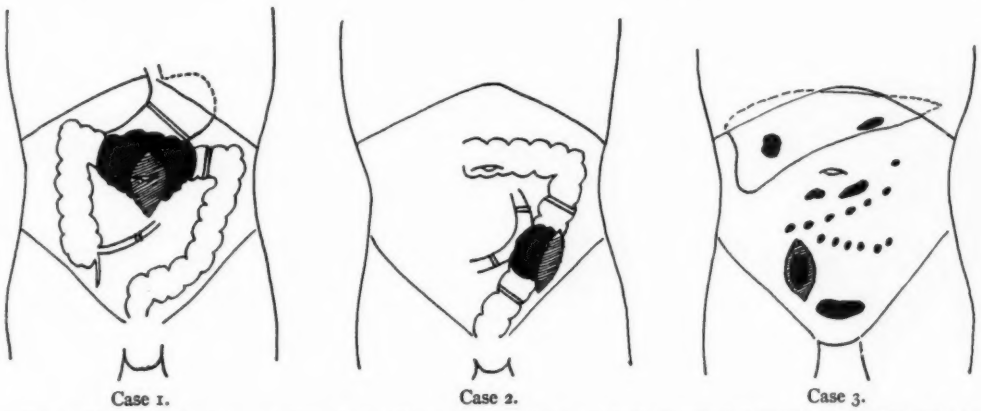

Fig. 1. Diagrammatic representation of operations performed in Cases 1 to 3. Black areas indicate carcinoma; shaded areas indicate extent of anterior abdominal wall involved by neoplasm and resected.

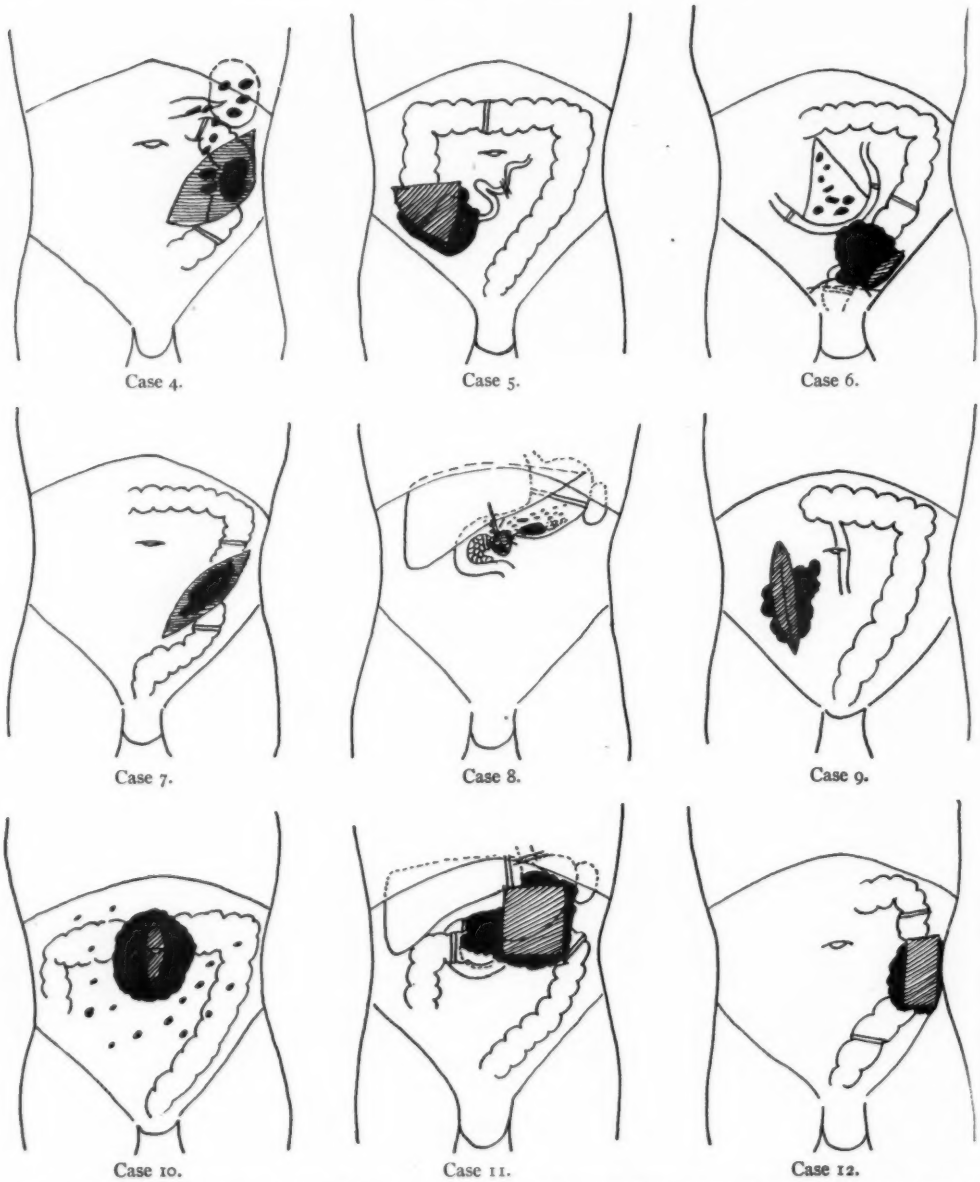

Fig. 2. Diagrammatic representation of operations performed in Cases 4 to 12. Black areas indicate carcinoma; shaded areas indicate extent of anterior abdominal wall involved by neoplasm and resected.

the lower ileum was resected *en masse* with the abdominal wall of the right lower quadrant for carcinoma primary in the cecum and infiltrating the abdominal wall. Ileo transverse colostomy was made. This patient is living and well 5 months after operation.

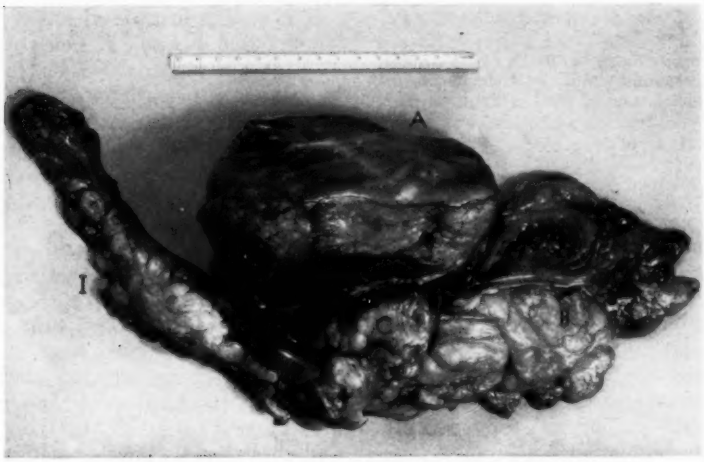

Fig. 3. Photograph of surgical specimen from Case 5 showing: *A*, large segment of lower right quadrant of abdominal wall including skin, subcutaneous fat and musculature infiltrated by *C* underlying carcinoma arising in cecum, *B*, ascending and transverse colon, *I* lower ileum.

CASE 6. P. Hel., no. 319547, male, aged 49 years. An exteriorization excision was done of the sigmoid bearing carcinoma, together with a long loop of the upper ileum invaded by carcinoma, as well as the mesentery of the ileal loop, the dome of the urinary bladder and the deeper portion of the anterior abdominal wall in the left lower quadrant. The colostomy was subsequently closed. Patient lived 14 months: returned to work for 8 months, but died of recurrences.

CASE 7. E. R., no. 160578, female, aged 48 years. An elliptical incision 11 by 7 centimeters was made in the left lower abdominal wall to include the mass of recurrent colon carcinoma (previous Mikulicz resection for primary growth) and the involved subjacent descending colon. A double barrel colostomy was made. Patient lived 10 months, then died of recurrences.

CASE 8. C. P. no. 325186, female, aged 55 years. Resection was done of the lower two thirds of the stomach, body of pancreas, spleen, periumbilical region of the abdominal wall, the falciform ligament for carcinoma primary in the body of the pancreas, with local spread and metastases to structures mentioned. Patient lived 4 months. She died of carcinomatosis.

CASE 9. E. L., no. 350135, female, aged 68 years. Resection *en masse* was done of previous lower right rectus incision scar with underlying mass infiltrating abdominal wall. Multiple small metastatic masses over the peritoneum also were excised. Patient lived 4 months, received palliation.

CASE 10. Gomol, no. 306534, female, aged 52 years. June, 1943 a supracervical hysterectomy and salpingo-oophorectomy for bilateral cyst-adenocarcinoma of ovaries were done. October, 1943, the periumbilical region of abdominal wall *en masse* with underlying and attached tumor 15 centimeters in diameter was excised. The latter was a large metastatic mass, the site of extreme pain. Patient survived 2 months. She died of carcinomatosis.

CASE 11. E. B., no. 339809, male, aged 28 years. Operation was carried out as follows; total gastrectomy, partial hepatectomy, partial pancreatectomy, transverse colectomy, spenectomy: resection *en masse* with the above, of the abdominal wall in the left upper quadrant, for round cell sarcoma (radioresistant). Patient survived 3 months: died of rapidly developing sarcomatosis.

CASE 12. C. B., no. 255457, male, aged 48 years. Resection *en masse* was carried out of cecum, ascending colon, right kidney and ureter, 70 centimeters of ileum and abdominal wall in the right lower quadrant for recurrent carcinoma of the cecum.

TABLE I.—SUMMARY OF RESULTS

Case 1	Living and well	4 yrs. 5 mos.
Case 2	Living and well	2 yrs. 5 mos.
Case 3	Living and well	2 yrs. 2 mos.
Case 4	Living but has hepatic metastases	1 yr. 2 mos.
Case 5	Living and well	5 mos.
Case 6	Lived	1 yr. 2 mos.
Case 7	Lived	10 mos.
Case 8	Lived	4 mos.
Case 9	Lived	4 mos.
Case 10	Lived	2 mos.
Case 11	Lived	3 mos.
Case 12	Lived	12 days*
Case 13	Lived	5 days†
Operative Mortality—2 Patients		15.4%

*Death from coronary occlusion.
†Peritonitis.

Patient died twelfth day postoperative. Necropsy revealed coronary occlusion.

CASE 13. C. F., no. 297424, male, aged 77 years. Exteriorization resection was done of the descending colon and the musculature of the left flank for carcinoma of the former invading abdominal wall musculature with abscess formation.

DISCUSSION

In all instances it was possible to close the wounds tightly following resection of portions of the abdominal wall. There were no wound disruptions. Soft rubber drains were inserted in some cases when suppuration associated with the parietal invasion was obvious. No definite recommendation may be made for these repairs since each procedure represents a special situation. The generally accepted principles of fashioning full thickness (skin, fascia, and sometimes muscle) sliding flaps are followed.

Three patients have survived over 1 year and are living, well, and returned to their usual occupations for an average of 36 months since operation. One patient, Case 4, received palliation for a year, having returned to his usual occupation but at this writing exhibits deterioration due to obvious multiple hepatic metastases.

The results in the series of 13 patients are summarized in Table I. One patient survived 1 year and 2 months, dying of metastases, but had returned to work for a period of 8 months. One is living and apparently well 5 months after operation. The patients who survived for shorter periods appeared to have received palliation although this was brief. Operation was performed in these patients because of pain and obstructive symptoms referable to the mass that was excised together with its parietal extensions. Some of the best results were achieved in patients with cancer of the colon which had invaded the abdominal wall. It has long been recognized that such carcinomas may evolve by local spread to adjacent tissues and viscera before distant metastases occur and these results are in accordance with this principle.

SUMMARY

Invasion of the anterior abdominal wall by carcinoma primary in an abdominal viscus does not necessarily indicate that the lesion is inoperable. Palliation and prolonged survival of the patient may follow extensive resections of such neoplasms with their parietal involvements.

OBSERVATIONS ON THE GENETIC NATURE OF GASTRIC CANCER IN MICE

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THE practice and science of medicine, being based exclusively or even predominantly upon the science of bacteriology, the conclusion is inevitable to some investigators that a cell or an individual is incapable of doing anything without being impinged upon by some external force. The science of genetics, stemming from the study of embryology, teaches differently. Genetics teaches that a zygote, that is, the fertilized egg, when placed in a suitable environment of temperature and humidity, given a few specific chemical entities, such as the essential amino acids and the vitamins, and a source of energy, is capable by development from spacially related internal nuclear entities or genes of giving rise to an adult plant or animal. This determination is so precise that many racial, familial, and individual characteristics are handed down from one generation to the next. This process of heredity has undoubtedly been going on from immemorial time and it probably will go on in the future, subject to change only by the sporadic appearance of mutations from time to time. It is the present intention to see whether this concept of biologic determination can also be applied to cancer, particularly to cancer of gastric origin.

In the first place, all cells of the body are derived by cell division from the zygote. Since cells and tissues reproduce physiological and morphological characteristics of their species in each and every generation, they must, of necessity, retain many potentialities from their zygotic origin. Superimposed upon this background of intrinsic determinations are many variations necessitated by environmental changes which are not, of necessity, hereditary. Now cancer is derived, by cell division, from some somatic tissue and, therefore, must retain some potentialities derived from the zygote.

The production of gastric carcinoma in mice was the result of the practical application of genetic principles by which the attempt was made to duplicate or to simulate in mice the variable biological state of the human population. For this purpose the genetic processes of hybridization and selection were used. In addition, however, each mouse received the subcutaneous injection of 1 milligram of methylcholanthrene dissolved in 0.1 cubic centimeter of sesame oil at 60 days of age. This procedure of injection has been followed for both parents for many generations. Beginning with the early hybrid generations the tendency to give rise to local tumors at the site of the injection of the carcinogen has been suppressed by keeping the descendents of the most resistant-to-cancer pair of mice in each generation. Due almost exclusively to this regimen of selection toward resistance to induced cancer there has been produced an increased latent period for the appearance of not only locally expected tumors but also of other types of tumors which appeared due no doubt to the fact that the selected hybrid mice with increased biologic variability, lived longer than they normally would following the injection of methylcholanthrene. Four stages or classes of mice based upon the classification of induced tumors have appeared in this selection experiment, as follows: (1) the appearance of tumors, such as epidermoid carcinoma and fibrosarcoma, at the site of injection of the carcinogen, (2) the surface spread of tumors over the entire body such as carcinoma of the mouth, the rectum, etc., (3) the appearance of tumors in the thoracic cavity such as adenocarcinoma of the lung, bronchiogenic carcinoma and mesothelioma, and (4) the occurrence of tumors appearing in the abdomen, such as primary carcinoma of the liver, liposarcoma of the uterine mesentery, lieomyosarcoma of the uterus and gastric

This experiment has been made possible by grants from The Jane Coffin Childs Memorial Fund for Medical Research and The Anna Fuller Fund. Presented in the symposium on Cancer before the Clinical Congress of The American College of Surgeons, Cleveland, Ohio, December 16–20, 1946.

carcinoma. Beyond these four stages where specific types of tumors occurred there was obtained a period, of short duration, in which no tumors appeared in spite of the fact that "an overwhelming dose" of a very powerful carcinogen had been injected. Even with continued selection toward greater resistance to all types of induced tumors, there occurred a reversal of susceptibility to induced cancer in which tumors appeared earlier and earlier in the succeeding selected generations. For the present purpose, however, we shall confine ourselves to the gastric carcinomas which began to appear in stage 4 enumerated above. These gastric lesions showed histological variability, some growing as polyps, while others grew invasively through the underlying muscular layers of the stomach. Metastases into the surrounding visera have also been obtained from these adenocarcinomas of gastric origin. When a suitable genetic experiment had been performed, it was demonstrated that the susceptibility to give rise to this gastric lesion showed linkage relationship with the gene that underlies brown hair pigmentation. Thus it is clear that a mutation has occurred on the brown chromosome sometime during the extent of the injection of methylcholanthrene into mice and that this mutation is responsible, in part, for the development of gastric carcinoma following the subcutaneous injection of methylcholanthrene. Another point of genetic interest is the fact that the untreated descendents of these mice which had developed gastric carcinoma following the subcutaneous injection of methylcholanthrene continued to develop gastric carcinoma spontaneously and they have continued to do so through eight untreated generations. At periodic times during the experiment of injecting both parents at sixty days of age with methylcholanthrene, a group of 120 mice have been separated off and kept under standard laboratory conditions without being subjected to any experimental procedure. In the succeeding groups of 120 mice referred to above the incidence of spontaneous gastric lesions and carcinomas increased in frequency and, at the same time, appeared earlier and earlier in life. Now there is available a strain of mice in which all individuals develop gastric lesions or carcinomas or some closely related biological entity spontaneously, the males, however, showing a greater susceptibility to gastric lesions than do females.

In addition to these gastric lesions of mucosal origin there has also been obtained several adenoacanthomas and squamous carcinomas of the forestomach which may serve as a source of material for other types of neoplasia induced by a subcutaneous injection of methylcholanthrene. In the gastric lesion, some of which are undoubtedly adenocarcinomas, it is clear that we have produced a hereditary disease or an inherited susceptibility to a disease by chemical means.

In his very excellent book on the "Foundations of Zoology" Professor W. K. Brooks had this to say, "if, like Paley, I kick a stone I may change its position, raise its temperature, and bring about other changes that might all be computed from a few simple data. What happens if, instead of a stone, I kick a dog? . . . What a difference between a kick against a dog and one against a stone! In one case the simple conditions may be stated in a few words, and the result may be computed; while in the other, a book would not suffice for the statement of all the facts, and the best science of our day is powerless to compute the result." This illustration is used to discuss the theme of the entire book of the relation of stimulus to intrinsic constitution in biologic response or behavior. Perhaps it is not too far-fetched to apply this concept to cellular physiology, especially to cancer. One may insult a cell by a multiplicity of agents such as bacteria, viruses, hormones and vitamins, but, in the last analysis, how the cell responds or even acts or fails to respond, is due, to no small degree, to its intrinsic genetic constitution determined, in part by its origin from the zygote. It is this genetic concept of the nature of intrinsic biologic variability together with chemical induction, that is making possible the development of many benign and malignant tumors in mice. A concept to be of value should, not only explain the contributions of the past, but should pave the way for new contributions. It is not out of place to point out to an assembly of surgeons that the cancer problem has not been solved and therefore we should not expect to find the

solution in the literature. Rather should it be desirable to advance in the study of cancer by producing more and more malignant conditions in experimental animals that duplicate or even approach the types of tumors that are killing more and more men and women at an ever-increasing rate. For this purpose the genetic concept of cancer has justified itself and should be of more than an academic interest.

In conclusion it may be pointed out that if genetic principles of hybridization, selection and inbreeding are capable of giving rise to a great multiplicity of tumor types, then the reverse of these same genetic principles should lead to the building up of a biologic state that will refuse to give rise to cancer in any form.

CORRELATION OF THE USE OF ANTIBIOTIC AND CHEMOTHERAPEUTIC AGENTS WITH GENERAL PRINCIPLES OF SURGERY

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THE introduction of potent chemotherapeutic and antibiotic agents challenged many traditional concepts in the surgical management of infections. A new group of nonsurgical specialists has arisen from the ranks of internists to concern themselves with the drug treatment of infections previously considered as surgical diseases. Paradoxically, this trend has not been correlated with a diminishing surgical responsibility for the treatment of impending or established infections. In fact, the net impact of this challenge has been the visualization of new fields for surgical exploitation. Entirely apart from the generally acknowledged necessity for the surgical drainage of pus, there are four major problems of clinical concern: (1) treatment of impending wound infection; (2) treatment of mixed infections due to both gram-positive and gram-negative bacteria; (3) treatment of the intravascular complications of bacteriemic infections; and (4) rôle of antibacterial agents in surgical management.

It is interesting that the dramatic accomplishments of the era of antibacterial therapy have so little altered the integrity of established and fundamental principles of surgery. Controversy has attended problems requiring surgical judgment, but control of the capricious quality of bacterial invasiveness has made more clearly evident the violation of fundamental biologic laws. The broad diagnosis of infection can no longer absolve errors in diagnosis, judgment, or technique. It is the purpose of this discussion to summarize the basic surgical principles validating this viewpoint.

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TREATMENT OF IMPENDING WOUND INFECTION

Experience in wound management among military surgeons in World War II crystallized much opinion about matters apparently still controversial among civilian and experimental surgeons. The major point at issue is the logic of local chemotherapy. Military experience justifies the abandonment of local chemotherapy in all wounds except occasional complicated wounds of serous cavities or major joints. Included in this philosophy of wound management is abandonment of the concept of prophylactic use of chemotherapeutic and antibiotic agents. Prevention of infection is an exercise in surgical technique. Antibacterial agents are reserved for the treatment of impending infection upon indications derived from clinical appraisal of the wound Thus, chemotherapy is solely an adjuvant to surgical competency in wound management.

Wound infection may be subdivided into two major components: invasive infection and wound suppuration. The invasive bacteria, capable of destroying living tissue, are the hemolytic streptococcus, toxigenic clostridium and staphylococcus. All are susceptible to penicillin therapy with occasional strain exceptions. Wound pathogens, responsible for wound suppuration, are a more heterogenous group and relatively resistant to currently available chemotherapy. In addition, the wound pathogens demand a nutritional pabulum other than living tissue within the wound. Devitalized tissue, blood clot and serous exudate in an open wound are removed naturally by septic decomposition; hence, the existence of such a pabulum is of greater clinical importance than the identity of the bacteria concerned with its liquefaction. The initial surgical care of the wound and the use of splints and pressure dressings are far more practical than attempts to sterilize residual dead tissue or exudate within the wound. In other words, the surgically clean wound requires no local chemotherapy and no amount of chemotherapy can sterilize an imperfectly débrided wound.

The living tissues of the wound are best protected from the ever present hazard of invasive infection by perfusion with a blood-borne antibacterial drug. Systemic therapy achieves this objective. It has been learned that the surgically clean soft part wound risks invasive infection only by the hemolytic streptococcus and that sulfonamide therapy adequately anticipates this danger. However, residual blood clot has been found as potentially acceptable as dead muscle as a nidus for clostridium infection. The greater antibacterial potency of penicillin for clostridium and staphylococcus makes it the drug of choice for wounds with residual hematoma or devitalized tissue. Such wounds are the complicated soft part wounds and compound fractures.

Again, clinical expediency has dictated the abandonment of routine bacteriologic culture of wounds as an index of infection. The gross pathologic appearance of the wound 3 to 10 days after initial surgical treatment is the best evidence of the adequacy of the initial excision and the presence or absence of infection. It is this general principle which underlies the two-stage technique of wound management. A further development of importance is the segregation of reparative and reconstructive phases of wound management. Postponement of reconstructive procedures to an elective schedule during convalescence and after wound healing has yielded greater success in ultimate rehabilitation.

TREATMENT OF MIXED INFECTIONS DUE TO BOTH GRAM-POSITIVE AND GRAM-NEGATIVE BACTERIA

Evidence for the minor rôle as wound pathogens of the gram-negative bacilli of the coliform group is gradually appearing. Even in peritonitis and bronchopulmonary suppuration, penicillin appears to be optimally effective when used in dosage adequate to control the gram-positive components of the infection. A similar conclusion has been reached in the study of wound infections.

This reasoning does not extend, however, to infections of the urine, bile, or cerebrospinal fluid. These body secretions contain an abundance of essential metabolites for bacterial growth and are deficient in sulfonamide inhibitors. Under the circumstances of mixed infection of the urinary, biliary or cerebrospinal system, the combination of penicillin and either sulfonamide or streptomycin may be desirable. To be effective, chemotherapy must be combined with restoration of normal flow for these systems.

TREATMENT OF THE INTRAVASCULAR COMPLICATIONS OF BACTERIEMIC INFECTIONS

The reduced mortality rate in bacteriemic infections offers the most convincing proof of the potency of presently available antibacterial agents. A consequence of this improved survival rate is an increasing incidence of residual complications of previously infrequent occurrence. Many unusual abscesses, such as the gas abscess of the retroperitoneal space as a complication of gas gangrene of the thigh, have been noted. Such abscesses rarely present problems in diagnosis or management. However, there are certain residual lesions of the vascular bed which are important for recognition and merit discussion as to principles

of treatment. These may be considered in two major categories: first, the intravascular foci of suppuration and, second, the metastases therefrom.

The intravascular foci of suppuration may be surgically accessible or surgically inaccessible. That surgical excision of all septic thrombi is not mandatory may be deduced from the experience with endocarditis and cavernous sinus thrombophlebitis. That conservative management is not uniformly successful is apparent from the experience with pylephlebitis. In the treatment of these lesions it is important to record the gradual abandonment of concomitant anticoagulant therapy in consequence of hemorrhagic complications.

The septic thrombi amenable to surgical attack are those associated with endophlebitis of the peripheral veins. Most frequently involved are the veins of the pelvic, jugular and saphenofemoral systems. The essential pathologic changes of septic endophlebitis render unlikely the detachment of a sufficiently large embolus to produce immediately fatal pulmonary infarction. Most commonly, progressive *septic infarction of the lung* and subsequent focal pneumonitis result. More rarely, there is an *extending thrombosis of a major venous pathway*. Such a process in the inferior vena cava with ultimate occlusion of the renal veins is associated with renal shut down and death from uremia. The life endangering qualities of these complications justify surgical intervention for any accessible focus of septic endophlebitis.

The possibility of septic endophlebitis is suggested by recurrent chills, spiking fever and persistent leucocytosis. The early diagnosis of progressive thrombosis or septic pulmonary infarction is not always easy. The septic emboli in the lung are usually microscopic in size and cast no shadow in the roentgenogram. The characteristic radiologic evidence of multiple, rounded areas of slightly increased density is dependent upon the development of pneumonitis around the areas of infarction. It is characteristic of these lesions that they progress to suppuration in spite of intensive chemotherapy. Tension pneumothorax, pyopneumothorax, empyema, and massive hemoptysis are features of this suppurative phase demanding appropriate consideration and treatment. Although the ultimate healing of multiple pyogenic abscesses of the lung is remarkably complete in the survivors, early venous interruption is the preferred method of treatment. Local tenderness over a likely venous pathway may be the only clue to the particular site of venous involvement. More rarely, the differential diagnosis of septic endophlebitis and endocarditis of the right side of the heart may require consideration.

Ascending septic thrombophlebitis of the inferior vena cava is usually a complication of an obvious focus of inflammation or abscess of the pelvis or lower extremity. The clue to caval extension of the septic thrombus is massive edema of the extremity at the time of iliac involvement.

As a general principle, it may be stated that excision of the affected segment is preferable to proximal ligation. Suppuration of the distal stump, such as occurs spontaneously in the veins of the face, may demand venotomy for drainage of pus. On the other hand, technical considerations dictate simple ligation of the inferior cava. This is readily accomplished through a rightsided retroperitoneal approach unless the necessity for concomitant interruption of the ovarian veins dictates a transperitoneal approach.

Another complication and a little emphasized feature of the successful treatment of endocarditis of the left side of the heart is the occurrence of mycotic aneurysms. Early diagnosis of these lesions is mandatory if surgical treatment is to be successful. No method of aneurysmorrhaphy is applicable to the septic and necrotic wall of these aneurysms. The only practical method of treatment is proximal ligation. Fortunately, many of these patients are sufficiently youthful so that adequate collateral circulation will develop after such an arterial interruption.

RÔLE OF ANTIBACTERIAL AGENTS IN THE OVERALL PROGRAM OF CLINICAL MANAGEMENT

The chronically ill patient depleted by persistent infection can rarely be cured by chemotherapy alone. This has been especially emphasized in the experience with actinomycosis wherein recurrences are prone to follow exten-

sive surgical excision and prolonged chemotherapy unless anemia is corrected by transfusion and body weight restored as part of the total program of management. The known toxic reactions and depressant effects upon hematopoesis, intestinal synthesis of essential metabolites and appetite combine to make the sulfonamides a questionable choice for the treatment of debilitating disease. From this point of view, penicillin is the drug of preference for intensive or prolonged chemotherapy.

It is significant that many of the untoward side effects of antibiotics and chemotherapeutic agents follow the pattern of drug idiosyncrasy and sensitizing phenomenon. There is good evidence that the route of administration of a particular antigen may influence the intensity and localization of subsequent allergic manifestations. Especially vulnerable in this regard is the bronchopulmonary system. It is not surprising that the incidence of acute asthma and tracheal edema has tempered the recent enthusiasm for inhalation of nebulized antibacterial agents for the treatment of pulmonary infections. Similar sensitization has been noted in consequence of cutaneous application of sulfonamides.

In general, it may be said that the incidence of toxic reactions increases with the duration of chemotherapy. Frequently, it becomes the obligation of the surgical specialist to assume responsibility for the differential diagnosis of toxic complications due to drug therapy and residual abscess or septic complications. The only practical solution to this enigma is earlier surgical consideration of the patient who fails to respond to chemotherapy. It cannot be emphasized too strongly that the period for optimal therapeutic response is rarely in excess of 5 days, even though longer periods of treatment may be desirable. Nor can the ultimate control of an infection in consequence of protracted chemotherapy be used to justify a completely nonsurgical program of management.

The point is best illustrated by reference to empyema. Sterilization of a pleural abscess without drainage may be followed by a degree of peripheral pulmonary fibrosis sufficient to cripple permanently the underlying lung. In other words, complete functional rehabilitation of the patient must not be sacrificed through concentration on the viability of bacteria within a focus of infection.

PHYSIOLOGIC ASPECTS OF SURGICAL INFECTIONS

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THE direct attack on the bacteria involved in surgical infections has been increasingly effective during the past 10 years. Scarcely a year has elapsed without bringing forth a new chemotherapeutic weapon better for some bacteriological purpose than those hitherto available. However, there is ample evidence to indicate that the proper management of infections calls for much more than the ritualistic administration of the right drug for the right organism. It seems appropriate in this symposium to recall attention to three primary reservations which should temper the purely bacteriological approach in the management of surgical infections: (1) Chemotherapeutic agents and antiseptics are only useful when they aid, rather than interfere with, the natural defense and recovery mechanisms of the body in infection, the process which Fleming calls "physiological antisepsis" (2) Effective management of many wounds infested with bacteria requires correction of an unhealthy physiological condition, rather than a direct attack on the bacteria. (3) In severe infections of almost all types there usually occur profound toxic functional derangements of organs and systems not immediately involved in the infectious process, and the chemotherapeutic agents administered will not of themselves serve to remedy the consequences of such disorders.

It is the purpose of this paper briefly to discuss these three aspects of surgical infections and to indicate that the use of our new-found weapons against bacteria must be handled with an understanding of their limitations, so that we may at all times recognize the ultimate importance of guarding and implementing the *physiological* mechanisms of recovery from infection, whether the infection be in a wound or a systemic invasive infection. The principles to be discussed are by no means new, in fact some of them were clearly recognized long before the discovery of the sulfonamides and penicillin. First will be considered some of the physiological aspects of treatment of localized tissue infections, or infected wounds, and next will be taken up the subject of toxemia in infection.

Sir Alexander Fleming, writing of the investigations on wounds during World War I, performed by himself and other members of a research team led by Sir Almroth Wright, made the following significant statement: "In view of the observations I have made, and which are quoted above, I venture to suggest that *the antiseptics at present in use will only exercise a beneficial effect in a septic wound if they possess the property of stimulating or conserving the natural defensive mechanism of the body against infection.* If such a thesis be true, then it brings the 'antiseptic' and the 'physiological' treatments on to the same basis, and it also makes it necessary, in the estimation of the value of an antiseptic, to study its effect on the tissues more than its effect on the bacteria."

The evidence in support of these assertions was largely drawn from a series of laboratory experiments on wounds *in vivo*, or on wound exudate *in vitro* with conditions which simulated as closely as possible the actual conditions existing in the wound. It was demonstrated that the ability of bacteria to multiply in wounds is conditioned to a very large extent by (a) the reaction of the exudate, loss of alkaline reserve being conducive to bacterial proliferation; and, (b) the antitryptic capacity of the serum or lymph; the presence of a low degree of antitryptic power tending also to encourage bacterial growth. Many bacteria lack the equipment of enzymes necessary to break down complex proteins into assimilable aminoacids and peptides, and the presence of active proteolytic enzymes in the bacterial environment presumably permits organisms of low

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virulence to undergo a parasitic adaptation which would not occur in a wound which is relatively free of active tryptic ferments. The proliferation of most types of bacteria in a wound is enhanced during the period of active digestion of slough by proteolytic enzymes which are thought to be derived principally from the disintegration of leucocytes in the wound exudate. According to Fleming this period of intense tryptic activity in the wound is accompanied by a rising level of trypsin inhibitor, or "anti-trypsin" in the blood. Once slough separation is complete and a complete covering of the wound with granulations has occurred, the discharges regain a high anti-trypsin titer (corresponding to that of the circulating plasma)—and streptococci and staphylococci predominate in the surface exudate. The duration of the period of tryptic activity may be shortened very materially by surgical removal of devitalized tissue, leaving that much less to the proteolytic action of the wound exudate. As soon as the devitalized tissue has been removed, either by natural or by surgical means, the conditions of the wound exudate will no longer favor the growth of bacteria which depend for their proliferation on the provision of proteolytic environment.

The other natural antibacterial mechanism to which Fleming called attention is the bactericidal capacity of leucocytes. In his experiments pus which had not stagnated in the wound for more than a few hours was found to retain a not inconsiderable capacity to destroy bacteria. The effectiveness of the leucocytes to kill bacteria depended on the provision of proper mechanical conditions for their ameboid movement over the wound surface; since leucocytes "crawl" and do not "swim," they will be relatively ineffective in a puddle of stagnant exudate, as in the lumen of a drain, and not at all effective in a mass of necrotic tissue; they will be most active in the wound where apposing surfaces have been brought firmly together so as to eliminate altogether the fluid filled spaces.

Recognition of these phenomena provides a sound basis for the application of physiologic methods to the management of contaminated and infected wounds. It becomes obvious that the primary consideration in both prevention and treatment of wound infections is to provide optimal conditions for the operation of the normal humoral and cellular defenses against infection. *Nihil nisi bonum* must indeed be the motto of every physician or surgeon who assumes the responsibility of handling wounds, and every contemplated method of treatment should be critically examined from this point of view before being applied. Surgeons no longer select an antiseptic for application to contaminated or infected wounds simply because the drug in question happens to have a strong killing or bacteriostatic action in the test tube against the organisms which infest the wound exudates. To paraphrase Sir David Willkie, what may be the joy of the bacteriologist is often the agony of the wound! Fortunately, penicillin and streptomycin, and to a somewhat lesser extent, the sulfonamides, meet the requirement of conserving, and even enhancing, the natural defensive mechanisms of the body. When administered in proper dosage and concentration, or applied to wounds in suitable form, they do not destroy leucocytes or tissue cells, they do not interfere with, and may even encourage, the natural separation of devitalized tissue, and do not delay the reparative process. The method of destroying bacteria in freshly contaminated wounds which Howes has recently advocated, involving the local use of combinations of Marfanil and streptomycin, would appear to meet the standards of physiological chemotherapy, and deserves extensive clinical trial. However, even these newly acquired agents of physiological chemotherapy must be employed with a sense of discrimination so as to recognize that many chronic wounds and ulcers, although heavily infested with bacteria, are not so much problems of infection as they are problems of tissue mechanics, blood supply, and wound nutrition. The empyema cavity which is not rapidly receding in volume under continued treatment with penicillin is much more a problem of tissue mechanics than it is one of infection, and the indicated treatment may be removal of the inflammatory structures which are preventing re-expansion of the lung, rather than further direct assault on the bacteria remaining within the cavity. The successful use in

chronic empyema of pleural decortication under the protection of penicillin demonstrates how a chemotherapeutic agent may aid the surgeon in attaining a physiological objective. In many long-standing leg ulcers the factor of superficial infection contributes to their chronicity, but success in eliminating the hemolytic streptococci, staphylococci, or colon bacilli will not alone allow the ulcer to heal if the poor circulation in the fibrous ulcer bed cannot sustain the growth and continued vitality of an epithelial covering. Permanent healing may await restoration of normal blood flow in the affected extremity, removal of scar tissue, and application of grafts of healthy skin. There is now ample evidence that chemotherapy and other forms of local treatment of large decubitus ulcers are gestures of futility unless the nutritional debility of the afflicted patient is first corrected, and when that has been done and all dead tissue removed, plastic closure of the ulcers can be performed successfully in the face of a very considerable amount of bacterial contamination.

The large scale clinical investigation of the use of topical sulfonamide applications in prevention of infection in civilian accidental wounds, which was carried on under the OSRD during the war, served to bring out very clearly the primary importance of the physiological condition of the wound, and emphasized the limitations of chemotherapy in meeting this problem. Conclusions from this study (3) were recently summarized:

"1. Factors tending to delay or interfere with wound repair, such as extensive tissue trauma, incomplete débridement, or improper or ill-advised closure with tension, residual dead-space, or implantation of foreign materials, will always predispose to the development of infection in accidental wounds.

"2. The use of chemotherapeutic agents in any combination and by any route does not prevent local infection of the wound when these predisposing factors exist.

"3. Chemotherapeutic agents are probably of great value in preventing invasive sepsis and death from infection following accidental wounds."

Therefore, the surgeon who attempts to lean heavily on the crutch of prophylactic topical sulfonamides in the performance of reparative surgery will sometimes be disappointed, and many of his good results will have been obtained in spite of, rather than because of, the application of the drug. However, there appears to be a valuable place for the local use of penicillin, and perhaps streptomycin as well, in the treatment of many established infections of wounds, in localized abscesses, acute empyema, suppurative arthritis and periostitis, meningitis, mastoiditis, and bronchiectasis. This practice is in keeping with physiological management if the antibiotic is also given intramuscularly in full doses to control such invasive aspects of the infection as may be present, and if the topically applied drug is dissolved in a suitable vehicle. The vehicle which has given the best results in cases under my own observation has been normal saline, containing 1000 to 5000 units of penicillin per cubic centimeter, administered either by intermittent aspiration and injection, as in acute arthritis and empyema, or, in the case of infected wounds, by intermittent irrigation through a very small indwelling tube which is held in place by the dressing or by loose gauze packing. In order to achieve the maximum effect, the drug must be applied so as to maintain a high concentration continuously in all parts of the wound.

Therefore, to summarize this initial phase of our discussion, the primary concern of the surgeon in the care of the localized infectious lesion should be to conserve and augment the natural mechanisms of the body for combatting infection. Surgical procedures can be of great value in removing tissues which have lost their capacity to react to infection, in improving blood supply, and in providing physiological conditions favorable to healing. Penicillin, streptomycin, and the sulfonamides will display their greatest value if used with proper discrimination in conjunction with surgery directed toward these ends.

The need for constant attention to the physiological mechanisms of infection is even greater in the management of severe invasive infections, such as peritonitis, septicemia, and gas gangrene, where their derangement seriously threatens the life of the patient. As one studies these infections at the bedside and in

the experimental laboratory, one is increasingly impressed with the similarity between the physiological condition of patients with severe infection and that of patients in shock due to blood loss, to crush syndrome, to intestinal obstruction, or to severe burns. Much of what has been learned about the prevention and treatment of shock during the last war may properly be applied to the treatment of patients with severe infections.

As used here, the term "shock" connotes an acute maladjustment in the distribution of sufficient available oxygen in the blood to meet the needs of critical organs of the body, particularly the liver, adrenals, kidneys, and heart muscle. Shock as so defined may be initiated not only by reduction of blood volume below that required for maintenance of circulatory dynamics, but also by loss of peripheral vascular tonus, by failure of proper oxygenation of the blood, and by a pathological alteration in the composition or physical condition of the blood.

Peritonitis perhaps illustrates the various aspects of shock in infection better than any other surgical infection because it brings into simultaneous interplay a number of factors which contribute to development of shock as it has been here defined. During the past 2 years I have had the opportunity of studying this subject extensively in dogs in the experimental laboratory, in collaboration with Doctors John H. Kay and Donald G. C. Clark (3, 9, 10). During the critical period of the disease salt and water are lost externally in vomitus, or in decompression of the paralyzed bowel, and internally into the edematous peritoneum and intestinal wall. Plasma protein is taken out of circulation in the process of formation of peritoneal exudate. Many red cells are destroyed by hemolysis, and others are lost from effective use as oxygen conductors by stagnation in the engorged vessels of the peritoneum and by the formation of sticky conglutinated masses of what Knisely has aptly called "sludge." All of these factors, unless corrected, contribute to the development of a progressively falling blood volume. However, replacement of the lost volume of blood does not necessarily relieve the shock state in peritonitis, a fact which was demonstrated during the war by Emerson and Ebert. One reasonable explanation of this is that the lysis of Gram negative bacteria present in the exudates of peritonitis permits the liberation of endotoxins into the portal and systemic circulations, which specifically impair the functions of capillaries and of cell membranes not only in the liver, to which these toxins are presumably carried in their most concentrated form, but in other essential organs as well (14, 15). Therefore, the shock state in peritonitis is probably compounded of reduced blood volume, plus the direct toxic action of products of bacterial and tissue origin. An interesting practical sidelight on the activity of endotoxins of Gram negative bacilli is the evidence now available from several sources (16) that the sulfonamides exercise a nonspecific protective action in animals against the lethal effects of such toxins. The beneficial use of sulfonamide prophylaxis and treatment of peritonitis may be attributable as much to this "antitoxic" action as to the repression of bacterial growth in the peritoneal cavity. We should therefore not be hasty to abandon entirely the use of sulfonamides in peritonitis in favor of the newer antibiotic agents, such as penicillin and streptomycin, until opportunity has been afforded to study more fully the comparative usefulness of these agents in combatting the factor of toxemia.

Still another physiological system which appears to be thrown out of balance in peritonitis is the equilibrium between the plasma proteolytic enzyme and its respective inhibitor. This is essentially the same system which Fleming was concerned with in his study of wound exudates, to which reference was made in the first portion of this paper. The proteolytic enzyme which is normally available for activation in plasma and which is most readily demonstrated through its lytic action on fibrinogen and fibrin, presumably exists for the most part in the form of an inactive precursor. However, just as is the case with pancreatic trypsin, which it resembles, the plasma protease may become converted to its active form through contact with activators of bacterial and tissue origin. The so called "fibrinolysin" of the hemolytic streptococcus is, in fact, merely an activator of the

plasma proteolytic enzyme system, and, in conformity with conventional terminology, has been renamed "streptokinase" (12). The action of the plasma protease is normally counterbalanced by a circulating inhibitor factor, corresponding to and closely resembling the pancreatic trypsin inhibitor. However, it was found (10) that in the crisis of peritonitis in the dog this equilibrium is thrown out of balance, and the "escape" of the lytic principle is evidenced by an increase in the lytic activity of plasma against both fibrinogen and fibrin. Lysis of circulating fibrinogen, and perhaps of prothrombin as well, appears to explain why the blood of animals and patients in shock from peritonitis and from other causes sometimes fails to clot. The work of Grob suggested a method of determining the significance of increased plasma proteolytic activity in the pathogenesis of peritonitis. He had shown that increasing the titer of protease inhibitor by repeated intramuscular injections or oral feeding of trypsin is accompanied by a marked increase in the ability of animals to withstand the local digestion of tissues caused by subcutaneous injection of proteolytic enzymes of animal and bacterial origin. My colleagues and I therefore undertook to evaluate the protective influence of repeated trypsin injections against the lethal sequences of appendiceal peritonitis, and obtained an interesting result. Peritonitis was produced in 18 pairs of dogs by appendiceal ligation; one of each pair had received daily intramuscular injections of crystalline trypsin for 12 days, and the other was a control. The management of the animals was in all respects identical, and the healthier-looking dog of each pair was always selected to be the control. The end-result was the survival of 15 trypsin-prepared animals, and of only 6 controls. The animals which had received trypsin preparation failed to display many of the morbid clinical and laboratory signs which were conspicuous in the controls. It may be added that efforts to influence the morbidity and mortality of the experimental disease in dogs were far less successful when chemotherapeutic agents were employed. The mortality rate in 15 dogs treated with large doses of penicillin was 33⅓ per cent (10). These experimental studies are mentioned here in order to indicate that there are important aspects in the morbid process of an established infection which are not likely to be countered solely by the administration of bacteriostatic chemotherapeutic drugs. We must continue to recognize that the infected patient is a more complicated system than a laboratory culture and that recovery from infections requires the stabilization or readjustment of many physiological disturbances which the infection has created.

Therefore, in treating the toxemia of severe infection, all possible use should be made of penicillin, sulfonamides, and streptomycin, but the fundamental physiological disorders that derive from bacterial infection must also be kept in mind, so that adequate supportive treatment, as well as chemotherapy, may be given. The following aspects of supportive treatment deserve particular emphasis:

1. Patients with serious invasive infections, including peritonitis, bacteriemias of all types, gas gangrene, and meningitis should be handled with the same concern for maintenance of blood volume as is employed in modern treatment of severe burns, and of hemorrhagic or postoperative shock. This will require generous use of whole blood, of plasma, and of saline and glucose solutions, guided by frequent estimations of hematocrit, serum proteins and electrolytes, and urinary output.

2. These patients should not be permitted to suffer from even temporary protein starvation. The patient with an acute infection is undergoing very active protein catabolism; the quantity of nitrogen excreted in the urine reflects a utilization of protein which is equivalent to three or four times the normal daily requirement. Still more is being continuously lost in the formation of inflammatory exudates. For example, a patient with empyema may be losing the equivalent of a pint of plasma each day in the form of purulent thoracentesis fluid. Unless an equivalent amount of protein is supplied in the diet, or by parenteral injections, a rapid depletion of liver and muscle protein is bound to occur, thereby undermining the resistance of the patient and aggravating the problem of his convalescence. All patients with infections should be maintained on a high protein, high caloric intake, and a

record should be kept of the amounts of food actually ingested. If oral feeding is contraindicated, protein should be given parenterally by a suitable hydrolysate, with glucose. The average adult patient should receive at least 125 grams of protein, and 2500 calories, daily.

3. The utilization and excretion of several of the vitamins is much increased during acute and chronic infections. After studying the requirements of patients in shock from various causes, Levenson and his associates have recommended the following daily doses of vitamins during the period of acute stress:

Ascorbic acid	1.0 gram
Thiamin	50 mgm.
Riboflavin	50 mgm.
Nicotinic acid	500 mgm.

After the period of critical illness has passed, these doses may be reduced to approximately one fifth of the above figures.

In view of the possibility that some of the physiological derangements in severe infections are related to inadequate storage of these vitamins, this aspect of balanced, supportive treatment should not be neglected.

4. Since the absorption of toxic breakdown products of bacteria and tissue is still the basis of toxemia in infection, much caution should be exercised before abandoning to chemotherapy exclusively the treatment of conditions in which surgical intervention has been our principal life-saving weapon in the past. The evidence may now justify the nonoperative treatment (1) of acute hematogenous osteomyelitis and other invasive infections where the susceptibility of the causative bacteria to penicillin may in most cases be assumed, but it is doubtful that chemotherapy will ever be more than a valued adjunct to surgery in the treatment of conditions such as appendicitis and its complications, and chronic pulmonary suppuration, and gas gangrene. Penicillin in large doses may be of definite value in established peritonitis following neglected appendicitis, as the recent report of Crile has shown but it will not compete with surgery as the principal treatment of choice in acute appendicitis.

SUMMARY AND CONCLUSIONS

1. Chemotherapeutic agents should be selected, and used, with a view toward aiding in the natural resistance of the body to infection.

2. Although it is important, wherever possible, to employ treatment directed specifically against the bacteria involved in an infection, the treatment of associated disorders should not be neglected. In certain conditions the persistence of the infection is entirely dependent on an underlying physiological lesion, and in these cases, chemotherapy is of only secondary importance.

3. Rational treatment of severe infections characterized by toxemia demands supportive measures as well as administration of chemotherapeutic agents. Particular attention must be given to maintenance of blood volume, provision of an adequate intake of protein, calories and vitamins, and surgical removal of the cause of the toxemia.

4. Study of the pathologic physiology of the toxemia of infections should be encouraged, in the hope that mortality from these conditions may be still further reduced.

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SYMPATHETIC INTERRUPTION IN CASES OF TRAUMA AND IN POSTTRAUMATIC STATES

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THERE can be no doubt that an erroneous impression has persisted from the past concerning the favorable influence of war upon medical progress. Actually the period of war must be recognized as having resulted in retardation of progress as compared with what might have come from a period of peace, whether measured by the health and longevity of the world population, the adequacy of undergraduate and graduate training of physicians, or the advancement of fundamental and applied knowledge. It behooves us then to salvage from the war effort all accomplishments which may be useful in the conduct of any future military engagement and more particularly those contributions which may aid in peacetime practice.

In the recent conflict not only was military medicine on a higher plane than in any preceding war but circumstances permitted a better evaluation of the preventive, diagnostic and therapeutic means which were utilized. Of especial importance in this regard was the creation by the Surgeon General of special centers for the care of certain types of injuries and disease, a plan which made possible careful study of these disorders and of their treatment under favorable circumstances by a group of medical officers competent for this task by special interest and professional preparation. Their study was, however, necessarily limited more or less to the later manifestations of these conditions, although prompt evacuation sometimes placed in their hands patients ill or disabled for only a few weeks. In addition, in spite of the difficulties resulting from the necessity for prompt evacuation of patients, certain deficiencies in facilities, and other circumstances arising from military demands, a considerable number of very informative reports have come from the Forward Areas. Such contributions naturally are attributable primarily to the proficiency and scientific interest of those who conducted them. Great credit must be given, however, to the Surgeon General's Office and to the consultant system utilized in the various theaters of command, and to their earnest, if not always successful, efforts to assign duties to medical officers according to their training and ability, to support them whenever possible with adequate equipment, and to stimulate the careful recording of case records.

The segregation of patients with vascular disorders and abnormalities involving sympathetic function in the Vascular and Neurosurgical Centers permitted a study of many of the problems for which sympathetic interruption has been recommended as beneficial in numbers rarely, if ever, before approached. This information has been supplemented by observations of these and allied conditions in Forward Areas. It is the purpose of this communication to inquire into the rôle of temporary and permanent interruption of the sympathetic nerves in the care of patients who have sustained trauma. No detailed analysis will be attempted, but rather a general presentation of the problem as it developed in my own experience and as it has been presented by other medical officers in the current American literature. For the sake of brevity I shall omit reference to the valuable work of numerous investigators whose contributions before the war established the principles and fundamental background for the application of sympathetic interruption in the surgery of warfare; one cannot emphasize too strongly the value of these investigations. Certain personal observations from the recent war have already been recorded in more detail elsewhere by my associates and me (26–29), and other reports

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covering sympathetic interruption in such conditions as the post-traumatic vasomotor disorders, cases of injury to major arteries, causalgia, and frostbite will be reported subsequently. The problems under consideration will be discussed primarily from the standpoint of the efficacy and the limitations of these procedures in therapy, whereas consideration of the often poorly understood underlying physiopathological mechanisms by which the sympathetic nervous system is involved as a component in these various states will be omitted.

In an effort to clarify the matter, the various traumatic conditions will be presented under several headings although it is realized that in any given patient the condition may not be a pure one, fitting precisely into any one of these categories but may have features common to several of them.

ARTERIAL STUPEUR OR SEGMENTAL ARTERIAL SPASM

It has long been recognized that trauma which actually inflicts no direct injury to an artery may initiate a reflex spasm of such degree that blood flow through this vessel may be interrupted, with resultant gangrene or ischemic paralysis in certain instances. Specific directives were issued giving proper instructions for the management of this condition. No large group of such cases is available for study. Presumably they were handled in the following manner: by periarterial sympathectomy when the artery was exposed in the course of débridement, and in all instances by prompt and repeated use of sympathetic blocks and other efforts to release vasoconstriction until permanent restoration of normal blood flow had been achieved. It is likely that a significant number of cases of segmental arterial spasm involving major arterial stems must have occurred among the thousands of cases of trauma to extremities. The best index of the efficacy of treatment is the fact that only a few instances of ischemic difficulties arising from this condition were seen in the Vascular Centers into which were funneled most of the patients with vascular injuries. These exceptional cases—tragic examples of loss of limb and of function without direct arterial injury—likewise serve as a stern warning for the necessity of prompt and proper treatment.

From the war experience it would appear that the following points are important in the management of this condition. Physicians must be aware of its existence and trained in its recognition. It must be considered a possibility in any case of injury in which the peripheral pulses in the limb have disappeared with resultant evidence of ischemia, and particularly when there is no significant external bleeding or hematoma and no sign of an arteriovenous shunt. It is important that operators be trained to recognize the spastic artery and differentiate it from other conditions following trauma, such as compression by hematoma or intra-arterial thrombosis. In general, the artery will be found to be pale and narrowed in caliber with good pulsation above the area of constriction and with weak or absent pulsation below. Generally there will be no hemorrhage in the artery wall. There will be no firm intra-arterial mass or distention of the lumen, conditions which are commonly observed in embolism or thrombosis.

Once the condition has been diagnosed or is suspected, every effort should be made to release vasoconstriction. If the artery is exposed at operation, its outer wall should be infiltrated with procaine and it should be carefully stripped of its adventitia. Warming of the body but not of the involved limb should be carried out. A sympathetic block or a spinal anesthesia should be done promptly. If vasodilatation and return of pulsations follow the block or spinal anesthesia but last for only a short while, sympathetic blocks should be repeated at frequent intervals. Should the benefit following each block be of short duration, one should not hesitate to proceed with operative sympathectomy, or with alcohol block if the patient's condition makes operation ill-advised. The limb itself should be protected from trauma and infection and should be left exposed to room temperature. Local warmth should never be applied unless there is conclusive evidence that one is dealing purely with a remedial condition of arterial spasm without any organic interruption of the continuity

of blood flow. If sustained return of normal blood flow is difficult to achieve promptly and there is no associated injury or disease contraindicating such treatment, anticoagulant therapy should be instituted without delay in order to inhibit thrombosis in the affected artery and in its collaterals.

No data are available as to the incidence of failures in patients who have been treated promptly and adequately; it may be anticipated that success will accompany such a program of treatment.

TRAUMATIC INJURY OF MAJOR ARTERIES

Though they did not constitute a considerable proportion of battle casualties, cases of direct trauma to major arteries presented a difficult therapeutic problem. Odom reported that there were 837 vascular injuries to major arteries among the 92,030 battle casualties sustained by the Third Army during a 9 month campaign in Europe, an incidence of 0.9 per cent. Four hundred and twenty-three of the 1833 amputations performed were necessitated by injuries to blood vessels (23 per cent). De Bakey and Simione stated that 0.96 per cent of 163,980 battle casualties were wounds of arteries, and 618 of the 3177 amputations from the Mediterranean and European Theatres were carried out because of arterial injury (19.5 per cent). In a smaller series of cases, Kirtley found that 20 per cent of major amputations were done because of inadequate blood supply. Bradford and Moore reported that 0.7 per cent of 16,000 surgical admissions to their hospital had injuries of important arteries. It may be concluded that slightly less than 1 of each 100 soldiers wounded in combat sustained an arterial injury and that approximately 20 per cent of all major amputations were performed because of trauma to blood vessels.

Medical officers were instructed by directive to utilize sympathetic blocks in all injuries of major arteries in which the circulation was definitely or questionably jeopardized. The results of this procedure, for obvious reasons, are difficult to analyze. The additional therapy in cases of arterial injury was never dependably identical. In some the concomitant vein was ligated while in others it was left intact. Although ligation and division of the artery were recommended, in certain cases ligation in continuity was performed. In some, an effort to maintain the continuity of the blood flow by suture or nonsuture methods was attempted, while in the majority no such efforts were made. In most instances adequate control of any attendant shock was promptly accomplished, but not in all. There was not uniformity in the application of measures to prevent infection and additional trauma nor in regard to the temperature to which the limb was exposed. Indeed, adequate sympathetic anesthesia was undoubtedly not always obtained by efforts to block the chain. Of equal import is the fact that sympathetic blocks were carried out as often as necessary in some cases and too few blocks spaced over too wide intervals in others. Of perhaps even greater importance in making evaluation of this procedure difficult is the varying character of the injury incurred.

In order to arrive at valid statistical conclusions, one would not only have to segregate treated and untreated cases according to the location of the arterial injury but would have to be certain that the two groups were comparable from the standpoint of the character of the local lesion, the associated trauma and the general state of circulation. Actually the extent of local trauma varied. In certain patients the artery was thrombosed without laceration, in others simply lacerated or severed, in still others badly damaged over a considerable extent. Sometimes there was extensive local trauma with injury to collateral vessels, extravasation, and edema, as well as associated fractures of varying severity or injuries to peripheral nerves. In contrast some patients had no associated lesion of any significant extent. Furthermore, in spite of efforts to the contrary, case records of patients were often deficient with regard to important factors concerning the character and the extent of the local and general injury and in regard to the therapeutic means employed. It must be remembered, too, that analysis of of the results of sympathetic interruption solely on a basis of the incidence of gangrene necessitating major amputation, as is sometimes done, omits consideration of possible effects of this treatment upon subsequent

occurrences of symptoms which may be annoying or even incapacitating. Furthermore it is of importance that sympathetic interruption was often reserved for the more serious cases in which threat of ischemic disaster was especially evident. As a consequence, mass statistical studies must be accepted with some question and there is little wonder that different analysts have arrived at diverse conclusions. It is apparent that the worth of the procedure can be estimated more reliably from the march of events in carefully studied cases.

In Odom's cases sympathetic blocks were performed routinely. In those patients treated by ligation of the artery the incidence of gangrene was 57 per cent, ranging from 44 to 86 per cent, according to the artery injured. He concluded that the results of sympathetic blocks were disappointing. Sympathetic blocks did not impress Bradford and Moore as beneficial in the cases they studied. In the series by De Bakey and Simione gangrene intervened in 39.3 per cent of 117 cases in which sympathetic blocks were used and in 48.8 per cent of 121 cases in which this procedure was not employed. Though the difficulties in interpreting these results were recognized they believed that the clinical course of patients confirmed the usefulness of sympathetic blocks in treating acute arterial injuries. In 42 cases in which sympathectomy was performed the incidence of gangrene was even higher (71.4 per cent), though it was felt that this occurrence was not indicative of the inefficacy of the procedure since many of these patients were treated after long delay or were cases in which the threat of gangrene was especially imminent. Kirtley had the impression that sympathetic blocks and sympathectomy were helpful. In a small series of cases, Freeman (10) found procaine blocks or alcohol block to be of benefit. Warren thought sympathetic blocks, or preferably sympathectomy, carried out before or immediately after ligation of arteries, were valuable aids. Mason and Giddings regarded sympathetic interruption as helpful, even though 8 of the 10 patients they treated by sympathectomy subsequently underwent amputation. Rose, Hess and Welch found it difficult to assay the value of sympathetic blocks in 100 cases of arterial injury, but did not find that it altered the outcome in avascular limbs from arterial severance, and felt that in only 2 cases was this procedure of importance in effecting a favorable result.

My own experience with a group of patients studied some weeks or months following injury to a major artery which had resulted in interruption of continuity either by thrombosis or by laceration and necessary ligation, emphasizes the hazard of statistical analysis of the results of early treatment from examination of the case records and the physical findings at a late date. Certainly some of the patients appeared to have benefitted from the procedure.

With regard to sympathetic interruption in an effort to correct certain difficulties which may follow traumatic division or thrombosis of arteries, I found in general that sympathetic blocks tended to result only in transient improvement, though there were exceptions, and that where sympathetic interruption was advisable in these cases, operative sympathectomy was the procedure of choice in the majority of instances. To summarize this experience, I may say that it was generally helpful in regard to such common difficulties as persistent evidence of sympathetic overactivity, coldness, cyanosis, hyperhidrosis, sensitivity of the part to cold, edema, pain, ischemic nerve palsies, poor muscular function, in the healing of persistent ulcers or minor amputation stumps, in improving the circulation in preparation for necessary plastic or orthopedic procedures, and in enhancing the chance of return of function in cases of peripheral nerve lesions. The resultant improvement was often dramatic. It would be incorrect to assume, however, that sympathectomy will bring about great or even small improvement in every instance when used to correct any of the difficulties enumerated above, with the exception of hyperhidrosis. In the group of cases in which Kirtley performed sympathectomy late for traumatic injury to arteries, he noted considerable improvement in the 3 patients who had intermittent claudication. Although improvement was sometimes noted in my series, in general

the exercise tolerance was not strikingly altered.

The results of sympathetic interruption in cases in which blood flow through a major artery was interrupted by trauma indicated this procedure to be of definite benefit, in my opinion; at the same time they clearly demonstrated that this procedure offered no guarantee against ischemic difficulties. With regard to civilian practice I believe the military experience would suggest that every lacerated artery be repaired, if this were possible, that sympathetic blocks be used promptly and as often as necessary, that when improvement with blocks is only transient, permanent sympathectomy be performed by operation if feasible, otherwise by alcohol injection. If sympathectomy is not carried out all additional aids in vasodilatation should be utilized such as reflex vasodilatation and the oral administration of alcohol. The limb is to be left exposed to room temperature and to be protected from injury and infection.

It is my impression that early sympathectomy will often prove helpful when procaine blocks are of little permanent help due to their transient benefit. In selected cases seen later after injury sympathetic blocks and, more often sympathectomy, will be found to be of considerable aid.

ARTERIAL ANEURYSMS AND ARTERIOVENOUS FISTULAS

Before the war sympathectomy or alcoholic infiltration of the sympathetic nerves had been used sufficiently often in cases of aneurysm and arteriovenous fistula to establish its usefulness as an adjuvant in their operative treatment. A number of surgeons during the war had occasion to employ sympathetic blocks or sympathectomy in such cases and held the opinion that they were useful aids. In the three Vascular Centers sympathectomy and sympathetic blocks were utilized in varying degrees. In general, these procedures were not employed at the Ashford General Hospital, and the brilliant results obtained there by Elkin and his associates furnish striking proof that large numbers of patients can be treated successfully without resorting to sympathetic interruption, though those of us who have studied patients after sympathectomy have been convinced of its usefulness. At the De Witt General Hospital sympathetic interruption was used fairly extensively and was thought to be very helpful in selected cases (11). At the Mayo General Hospital a great many sympathectomies were performed. This experience has permitted me to evaluate the procedure carefully and to formulate certain concepts concerning its benefits and its limitations.

Sympathectomy tends to render the collateral circulation more efficient by elimination of vasoconstriction in the collateral vessels. Though sympathectomy may also contribute to improvement in circulation by fostering growth of new collaterals and though certain observations suggest that this may be true, convincing proof has not been demonstrated. When the collateral circulation appears insufficient according to carefully performed tests, when a sufficient time has elapsed to have ordinarily brought about adequate collateral circulation, and when such means as intermittent occlusion of the artery appear to be achieving little or no improvement, sympathectomy is indicated. It is also indicated in all cases with poor collateral circulation in which intense pain, infection, or threat of rupture make the necessity for early operation a real possibility. In the majority of cases the collateral circulation will be found to be adequate immediately or shortly after sympathectomy. In a number, however, the tests for collateral circulation may show improvement but may not become adequate over a period of months. Because sympathectomy has been accomplished one can in no sense assume that the collateral circulation will be invariably satisfactory or that gangrene or ischemic paralysis will always be prevented.

Sympathectomy is indicated in any case in which an aneurysm or fistula is associated with a peripheral nerve lesion and in which the collateral circulation is precarious; indeed in any case with severe peripheral nerve injury and obviously impaired circulation, regardless of whether tests for collateral circulation are satisfactory or not. It appears wise to do everything in these cases to make possible

early surgical treatment of the aneurysm or fistula in order to avoid delay in operating upon the damaged nerves. Occasionally one will find it advisable to perform sympathectomy as a safeguard in cases of vascular lesions of important main stem arteries when the location of the lesion makes accurate compression of the artery and testing of the collateral circulation impossible. It appears rational to perform sympathectomy in those cases with ischemic lesions distal to an aneurysm or fistula. It is indicated when there is significant vasospasm in the affected extremity. The procedure may occasionally be advisable when one or more of the important arteries in a limb have already been ligated or thrombosed and in which cure of aneurysm may entail ligation of other important arteries or collaterals. Sympathectomy may sometimes be required because of associated causalgia.

Sympathectomy need not necessarily be performed before operation; the two procedures can often be carried out in one session. In every instance, however, one should retest the collateral circulation after sympathectomy and make certain that it is satisfactory before proceeding with the surgical treatment of the aneurysm or fistula.

After operation, sympathectomy will also be found to be an adjuvant in correcting certain difficulties which sometimes follow extirpation of an aneurysm or fistula. It is clearly indicated when there is annoying or incapacitating sensitivity of the hand or foot to cold in a patient whose place of residence and work or avocation make such exposure necessary, and when improvement in symptoms is noted on exposure to cold during a period of procaine sympathetic anesthesia. It is useful in cases of persistent edema which have not improved upon conservative treatment. It is generally helpful and often dramatically so in cases of ischemic paralysis. It appears to foster return of nerve function in cases of peripheral nerve injury in which the circulation is impaired. It is also useful in the treatment of associated causalgia which is improved temporarily but not cured by sympathetic blocks. When a limb is found to be cold and pale or cyanotic after operation or when gangrene is definitely threatened, sympathectomy should be utilized; in some cases it brings about gratifying restoration of good circulation though it will not always prevent gangrene. In regard to the two commonest circulatory disorders which may follow sympathectomy, sensitivity of the limb to cold and decrease in exercise tolerance, the procedure has a very beneficial effect upon the former but rarely has a striking effect upon the latter.

It is my feeling that when sympathetic interruption appears to be indicated, permanent sympathectomy is generally preferable to procaine blocks, though blocks undoubtedly have a place in the treatment of certain cases. Sympathetic interruption seems justified for the indications which have been enumerated; where no clear indication exists there seems to be no point in performing this procedure. It must be looked upon as a valuable adjuvant in the surgical treatment of aneurysms and fistulas. It cannot be relied upon as a certain guarantee against ischemic difficulties, nor can it be relied upon as a sure corrective for all functional disorders which may be present.

To have performed a sympathectomy does not relieve the surgeon of responsibility for utilizing carefully performed tests for collateral circulation, for exercising every care to prevent destruction of collateral vessels at the time of operation, and for preserving the continuity of the artery if possible.

THE POSTTRAUMATIC DISORDERS

The posttraumatic vasomotor disorders comprise a number of conditions about which many divergent opinions are held. Some would include only those cases with edema, pain, weakness, disability, atrophy, osteoporosis, and either vasoconstriction or vasodilatation. Others would include in this category various vasomotor disturbances following trauma, infection, and such vascular disorders as thrombophlebitis. The discussion here will be limited to the difficulties following trauma or to trauma and associated infection. It has been my experience that these disorders may be characterized by various complaints and physical findings. In some

pain is present, either at rest or more commonly with activity and weight bearing; in others pain is absent. In some edema is massive, in others moderate or mild, and some have no edema at all. Some have evidence of vasodilatation, the majority, of vasoconstriction. Cyanosis, coldness, sensitivity of the part to cold, and hyperhidrosis may be present in varying degree. Some have marked weakness of muscles, some virtual paralysis. Sensory changes may be present.

In a group of disorders so varied in their manifestations there is little wonder that treatment cannot be stereotyped and that results of therapy are not uniform. Those who have utilized sympathetic blocks and sympathectomy have been favorably impressed with the results of such treatment (32), as have my associates and I. It is not my feeling that such treatment should invariably be applied or that it can ever be utilized as the sole means of therapy. It is difficult to outline concisely one's views of treatment for such a complex problem but to do so as succintly as possible, the following suggestions are made.

In any case of trauma which is unassociated with injuries contraindicating such treatment, early active use of the part should be instituted. Obviously, wounds must be débrided, fractures properly reduced and immobilized, and every precaution taken to prevent infection. Whenever edema is present proper elastic support, elevation and gradually increasing use of the limb in dependency should be utilized. One must be sure to encourage the patient and to do everything to prevent development of an attitude of invalidism. If a real neuropsychiatric factor exists, it must be recognized and suitable treatment instituted.

Whenever there are signs or symptoms suggesting a reflex disturbance such as is under consideration and these manifestations prevent active use of the limb or do not improve rapidly with such activity and with proper associated treatment, sympathetic blocks should be tried without delay and should be repeated as frequently and as often as necessary. If they bring about transient improvement but appear to have no permanent benefit, one should not hesitate to proceed with sympathectomy. In certain cases it will be preferable to employ local procaine infiltration first before performing sympathetic blocks. If such local infiltration brings about temporary benefit but no cumulative improvement and an irritable trigger zone seems to exist which can feasibly be excised, such a procedure may be indicated. In connection with local infiltration, it is proper to introduce here the technique of procainization in the early treatment of sprains and strains which was found very effective in army personnel (20). That at least part of this benefit results from blocking the sympathetic impulses is suggested by the fact that such injuries have been treated with equal success by sympathetic blocks (32).

In the treatment of the late sequelae we have found that many patients obtain an excellent result from active use of the limb, physiotherapy and elastic support when needed. It was found that in a small number of patients manifestations very similar to those generally observed were either initiated or perpetuated by neuropsychiatric factors. In such cases psychiatric therapy is obviously required. In some a brilliant result is quickly achieved; others are very refractory. In rare cases responding unsatisfactorily to psychiatric treatment, sympathetic interruption may be a useful adjuvant in correcting certain manifestations such as persistent massive edema. When the simpler means of treatment show no promise, sympathetic blocks should be carried out. Occasionally a patient is helped decidedly by blocks, but ordinarily any beneficial effect is transitory. In general, sympathectomy is the procedure of choice for such cases. Except for cases in which a fundamental psychiatric problem has been unrecognized before operation, the results are gratifying. The manifestations of vasospasm and sympathetic overactivity respond dramatically; cyanosis, coldness, hyperhidrosis are relieved and sensitivity to cold is cured or improved. Edema is generally lessened, sometimes dramatically. Pain is generally improved and is sometimes completely eliminated. Sympathetic interruption can never be regarded, however, as the sole

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form of treatment. Whether it is used or not, the patient must be encouraged, active exercise must be enforced, and edema must be dealt with by elastic support, rest, and gradually increasing dependency.

No data have been made available in regard to possible usefulness of sympathetic interruption in the healing of fractures. It has been demonstrated, however, that sympathectomy may be extremely useful in reducing edema and in eliminating marked vasospasm before bone grafting and other plastic restorative procedures.

CAUSALGIA

The war afforded an unparalleled opportunity for studying large numbers of cases of causalgia and their treatment (2, 12, 18, 24, 31, 33). In general, excellent results from sympathectomy were obtained. The majority of patients obtained complete relief and improvement was almost invariably noted in the remainder. It has been the common observation that the results were better in the upper extremity than in the lower. Certain observations suggest that the poorer results in the lower extremity may be due in part to incompleteness of the ganglionectomy—that it may be necessary to sympathectomize completely the area of the nerve lesion as well as that to which the pain is referred (2, 33). The series of Rasmussen and Friedman suggests that postganglionic operations for the upper extremity are inferior to the commonly employed preganglionic operation in the treatment of causalgia. Although such observations have not been uniformly made, it has been my experience that the more severe the pain the more apt one is to obtain complete relief following sympathectomy. Since the pain is generally more severe in the upper extremities this may be an additional factor in the somewhat higher incidence of complete cures in these cases as contrasted with those having involvement of the lower extremities. In general, it is thought that the results are more favorable the earlier treatment is instituted.

Some surgeons have utilized sympathetic blocks only as diagnostic and prognostic tests and some (33) have never obtained permanent relief from any number of procaine sympathetic blocks. Though we found that sympathectomy was necessary in the majority of cases, my associates and I observed permanent relief from sympathetic blocks in numerous instances. It is our feeling that one should proceed with sympathectomy if relief of pain is limited to the period of sympathetic block and that a series of blocks should be tried in patients who experience prolonged relief after a procaine block. If the relief does not become progressively more prolonged as additional blocks are carried out, they should be abandoned and operation should be carried out. It is apparent from the experience in the war that a rare patient with causalgia may be cured by neurolysis or neurorrhaphy or by artificial fever therapy. A rare case, too, may be associated with definite neuropsychiatric features and respond favorably to psychiatric therapy (16). In general, however, sympathectomy is required. Altogether the results are brilliant.

PHANTOM LIMB PAIN AND AMPUTATION STUMP PAIN

Few wartime observations have come to my attention concerning the use of sympathetic interruption in the distressing phantom limb syndrome and in amputation stump pain. To be sure, a few cases of pain and vasospasm in minor amputation stumps with improvement or relief following sympathectomy have been recorded (12) and I have made similar observations. In addition, Pool has used sympathectomy in conjunction with cordotomy in a few cases of phantom limb pain and has the impression that sympathectomy may be helpful in relieving the burning pain seen in this syndrome. In general, however, no studies have been made of sympathetic interruption in the complex amputation stump pain following major amputations nor in the phantom limb syndrome—in all likelihood a reflection of the infrequency with which these difficulties have occurred in military personnel. I believe the primary lesson to be learned from the experience in the recent war deals not with the treatment of amputation stump pain and phantom limb pain but with their prevention by proper operative technique, by early active

use of the stump, and by careful conditioning of amputees to the normal physiological sensations of a phantom limb which they almost invariably experience (19). I have had occasion to observe in patients in whom such procedures were performed for other reasons, that the normal phantom limb sensations may be temporarily but not permanently relieved both by sympathetic blocks and by sympathectomy. My own small experience would lead me to believe that sympathectomy rarely has a place in the treatment of amputation stump and phantom limb pain.

THE INJURIES DUE TO COLD

Opinions are at wide variance in regard to the rôle of sympathetic interruption in the injuries due to cold—frostbite, trench foot, and immersion foot or hand. Elsewhere (28) I have attempted to review this subject. It appears clear that although other factors may have a part, thrombosis of arteries and arterioles is the primary factor concerned in the production of gangrene—the most disastrous sequel to injuries from cold. It is further well established that vasoconstriction is the primary response of the body to exposure to cold, and that, although a transient period of reactive hyperemia may follow, vasoconstriction is one of the commonest sequela. These facts would suggest that efforts to block sympathetic impulses and combat vasospasm might be fruitful in the treatment of the acute and later manifestations of these disorders.

Numerous students have advised against sympathetic interruption in the early stages of trench foot, immersion foot, and frostbite, perhaps on insecure grounds. There is little information from our own war experiences concerning the effect of these procedures in the early treatment of frostbite although some of our allies and opponents reported good results with sympathetic blocks and periarterial sympathectomy. Davis and associates, who felt that it was important to release vasoconstriction as rapidly as possible, found that direct blocking of the sympathetic pathways was the only means of accomplishing this end in severe high altitude frostbite. Southworth has treated a few cases of early frostbite by sympathetic blocks with apparent benefit. Berson and Angelucci noted no improvement with sympathetic blocks in a few early cases of trench foot with massive edema, but obtained temporary diminution of pain and tenderness in milder cases. Leigh reported that sympathetic blocks were of no aid in the early treatment of trench foot. Edwards and his co-workers, in a small group of cases, found that sympathectomy gave good results in the early treatment of trench foot with gangrene but that it was not helpful in cases with tender, painful, and aching feet. No studies have come to my attention concerning the use of sympathetic interruption in the treatment of the acute phases of the immersion injuries.

With regard to treatment of late manifestations of these disorders, the rôle of sympathetic interruption has been more clearly defined. The results of sympathectomy are good in properly selected cases of frostbite. The procedure is useful in cases of gangrene, excessive hyperhidrosis, persistent marked vasospasm, sensitivity of the hand or foot to cold, and sensory changes. Southworth reported some observations suggesting that repeated procaine blocks, alcohol blocks, or sympathectomy may be helpful. Berson and Angelucci reported that sympathetic blocks were useful in late cases of trench foot with vasospasm, and that the improvement in treated limbs was faster than in the nontreated contralateral extremities. Although my associates and I were not impressed with the usefulness of sympathetic blocks in the late treatment of trench foot, we obtained conclusive evidence of the benefit of sympathectomy in selected cases. Sympathectomy, unfortunately, rarely is of aid in alleviating the pain which is so commonly experienced on weight bearing. It is particularly helpful in cases of gangrene, in marked hyperhidrosis, especially if associated with maceration of the skin and secondary infection, in reducing the severity of symptoms in patients with sensitivity of the extremity to cold, and in certain cases in which there is disturbance of sensation. Patterson found that sympathetic blocks improved temporarily the peripheral pulses, decreased numbness and pain, and abolished hyperhidrosis in the Attu casualties,

but observed that the beneficial effect was limited to the duration of sympathetic anesthesia. Southworth felt that sympathectomy produced beneficial effect upon the late manifestations of immersion foot although it had little effect upon deep pain.

Because such contradictory opinions are held by different observers, it is exceedingly difficult to summarize any lessons which may have been learned in the recent war concerning sympathetic interruption in the treatment of the early stages of the injuries due to cold. I think it is fair to say that at least no harm has resulted from the use of such procedures and that their use for further evaluation is warranted. There is much to suggest that they may be very helpful, especially if applied early, and particularly in cases in which gangrene is threatened or existent. It is my feeling that if transient improvement without permanent benefit is noted following blocks, especially in cases with marked ischemia, one should seriously consider early sympathectomy. With regard to the later stages of these injuries, it is clear that sympathectomy has a definite though limited place in therapy. Though repeated sympathetic blocks may occasionally result in benefit, sympathectomy is generally required. Sympathetic interruption cannot be looked upon in any case as the sole means of therapy. One must, under all circumstances, protect the injured limb from trauma, infection, and from external heat in the acute phase; there is much to suggest that anticoagulants should be employed in early cases; conservatism should be practiced with regard to gangrene and necessary amputations; physiotherapy and active exercise should be utilized after the acute phase is passed; shoe corrections, psychotherapy and other means should be used when indicated. It is my opinion that further experiences will confirm the usefulness of sympathetic interruption in alleviating certain complaints late in the course of these disorders and that they may well prove of value in the early stages.

SUMMARY AND CONCLUSIONS

The experiences during the recent war have in general confirmed pre-existing impressions concerning the usefulness of sympathetic interruption in cases of trauma and in the posttraumatic states. Certain new applications of these procedures have been established. The war experiences have been particularly valuable in providing large numbers of cases for study with consequent better evaluation of the specific indications, the merits and the limitations of sympathetic interruption. It would seem that permanent sympathetic interruption may yield gratifying results in some instances in which procaine blocks give unsatisfactory results. With regard to certain types of injury, there are differences of opinion concerning the usefulness of these procedures. In the presentation of this problem an effort has been made to take into consideration the studies of various investigators, though the views expressed concerning controversial issues have necessarily been influenced by personal experiences.

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THE TRANSPORTATION OF SOLDIERS WITH FRACTURES

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THE transportation of a soldier with one or more fractures, usually compounded, was one of the major medical problems encountered in the European Theater of Operations. In general, most of the patients, immediately after wounding, were transported by ambulance from the aid stations to the forward hospitals, and then by train, boat, or airplane to the rear echelon hospitals.

The past standard practices of transporting patients with fractures recommended by the Army Medical Corps were reviewed by the consultants and somewhat modified before the advent of major hostilities on the continent. The major modification was made in regard to the transportation of fractures of the upper extremities.

Almost everyone consulted agreed that the Murray-Jones arm splint was an awkward device to apply, and it was felt by most doctors that this awkwardness, combined with certain dangers of excessive pressure in the axilla, offset any good factors about the splint. Accordingly, the medical officers were not encouraged to use it. Most upper extremity injuries were very simply and easily handled by simply binding the affected arm to the trunk with a sufficient number of triangular bandages. This provided good, comfortable immobilization and obviated the necessity of applying a cumbersome piece of apparatus. In addition, transportation by litter in an ambulance was a much simpler procedure than it would have been if this splint had been used widely.

Upon arrival at a field or evacuation hospital, or any hospital where surgery on the injured upper extremity was performed, a plaster velpeau or modified plaster shoulder spica dressing was applied after surgery and was termed a "transportation plaster splint" for the next stage in the evacuation of the patient.

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This splint was either removed and the wound was inspected and the splint then was reapplied, or else it was left intact by successive medical officers in the line of evacuation, according to their best judgment. Eventually, the patient reached a general hospital where he was to be hospitalized for the next stage in his treatment. At this hospital the "transportation plaster" was removed and appropriate therapy, usually skeletal traction, was instituted to care for the fracture.

The first splint applied for the transportation of fractures of the long bones of the lower extremity was almost universally the army half-ring splint. This was applied at the forward dressing station and remained in place until the patient was received at the field or evacuation hospital for his initial definitive therapy. The ambulance drivers and others responsible for his care during transportation from the aid station to the forward hospital were instructed to release the traction provided by the army hitch which was, in most instances, applied over the patient's shoe of the affected extremity. In the event the foot had been injured together with the long bones of the lower extremity, the extremity was simply held in place in the half-ring splint by means of triangular bandages, usually five in number, and no attempt was made to apply traction. I observed a few individuals arriving at evacuation hospitals who had had undue pressure caused by the army hitch, or who had had the hitch in place many hours without release, but I cannot recall a single instance where any permanent damage was done by this procedure. I was favorably impressed by the comfort with which most soldiers with extensive fractures were transported from forward aid stations to evacuation hospitals in the army half-ring splint.

After initial definitive treatment—débridement, etc.—at the field or evacuation hospitals, these patients, for the most part, were encased in one and one-half plaster hip spicas for a

single extremity, or double spicas when both legs were involved, and removed to the next hospital in the line of evacuation. These spicas were very well padded affairs. Plaster and padding were split and cut down to the skin throughout the entire length of the extremity up to the hip joint on the affected side; the legs of the plaster were joined with one or more plaster ropes or wooden struts to provide for stability. The patients who were received at rear echelon hospitals in all of these "transportation plasters," both for the upper and lower extremities, were for the most part remarkably comfortable, shock was minimized, pain was not an outstanding complaint, and dressings over the operative areas were retained in place, requiring minimal attention and inspection.

Before the advent of major hostilities in Europe, the American Army Medical Corps was given the experience of the British in regard to transportation plasters. The British recommended the use of a hanging plaster for fractures above the elbow joint and the use of Tobruk splints for lower extremity injuries.

The hanging plaster was found by most American medical officers to be unsuitable because it did not immobilize the fracture during a long rough ride on a litter in an ambulance. Most patients complained of pain. The Tobruk splint was not regarded favorably by American medical officers because of the lack of immobilization of a fracture of a femur unless it happened to be just at, or immediately above, the knee joint, and because of the consequent pain the patient experienced.

I, myself, tried on many occasions to demonstrate a Tobruk splint to American medical officers and had a most difficult time applying it, much more trouble in fact than was experienced in applying the large one and one-half or double plaster transportation hip spica.

There were many modifications of the Tobruk splint but, in general, it consisted of:

1. Adhesive traction straps applied to the skin along the full length of the extremity, with padding over the malleoli.

2. An overlying snugly applied long-leg plaster splint, encasing the foot, to provide support and minimize rotation of the extremity.

3. Slots in this plaster in the region of the malleoli through which the traction straps were passed.

4. An army half-ring splint supporting the whole extremity in plaster with the traction straps tied over its end.

5. The incorporation of a windlass arrangement in these straps, theoretically to provide skin traction to the injured extremity.

Undoubtedly, the British transportation plasters, namely, the hanging plaster and Tobruk splint, used less material than did the American army's spicas and velpeaus, and also could be applied with the aid of less personnel, but the patients were definitely not as comfortable as in the American devices. The British medical units had less material and fewer personnel than did the American counterparts, and it is my own feeling that these transportation splints were developed to meet the material and personnel shortages of the British Army.

The Tobruk splint was used upon occasions by American medical officers and an attempt was made by one of the army consultants, Lieutenant Colonel John Manning, to follow up all of these cases in the Ninth Army. The number of cases that he was able to contact was nowhere near as impressive as the British figures but the conclusions reached by Lieutenant Colonel Manning substantiated the general belief that: (1) There was no uniformity in the types of splints used; (2) the transportation of such patients was accomplished with much more pain and discomfort than those encased in plaster spicas; (3) the problem of retaining dressings in place in the upper thigh was much more difficult then when a spica was used.

Translating these lessons to civilian life, it seems to me perfectly logical to recommend the abandonment of the use of the Murray-Jones arm splint as a first aid appliance. I believe civilian patients can have upper extremities, particularly when the humerus is involved, bound rather snugly to the trunk by gauze or elastic bandages and can be transported in comfort. I should certainly recommend the use of a plaster velpeau type of dressing, if a compounding wound has been suffered which has been débrided or closed, in

a patient who must be transferred to some other hospital for long-term care. When civilian injuries involving the long bones of the lower extremities are encountered, the army half-ring splint with foot-piece and army hitch, reasonably well padded over the dorsum of the foot, provides an excellent device for transportation. In the event a compounding wound has been encountered which has been débrided or closed, a well padded plaster spica applied to the extremity, without regard to the problem of reduction of the fracture, serves as an excellent transportation device.

CONCLUSIONS

1. The Murray-Jones arm splint was felt to be cumbersome and difficult to apply. Much more comfortable and efficient immobilization was obtained by binding the injured upper extremity to the patient's trunk.

2. The plaster velpeau and modified shoulder spicas were preferred to hanging plasters in transporting patients after initial surgery.

3. The army half-ring splint with army hitch is an excellent device for transporting fractures of the lower extremity.

4. One and one-half or double hip spica plasters are recommended after initial surgery and are much to be preferred to the British transportation devices labelled Tobruk splints.

5. The above devices, consisting of patient-body immobilization, plaster velpeaus or shoulder spicas, army half-ring splints with foot-rest and army clove hitch, and plaster transportation spicas can well be recommended for civilian use.

PENICILLIN IN EXPERIMENTAL INTESTINAL OBSTRUCTION

A Summary of Observations with Reference to Their Clinical Application

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THE mechanism of death in intestinal obstruction is only poorly understood. Previously, death in all types of obstruction was ascribed to a toxemia. It is now known that the vomiting associated with high obstructions produces profound chemical changes in the body and that these may be alleviated by the parenteral administration of salt and water. The studies of Wangensteen and others have shown that the relief of intestinal distention does much to reduce associated shock and the hazards of operative intervention. In spite of the advances of recent years in the management of bowel obstructions, we still find 1 patient out of every 5 or 6 dying after operation for acute, mechanical obstruction of the small bowel (5).

It is thus obvious that more must be learned concerning the pathology of intestinal obstructions in order that new surgical adjuncts can be developed to diminish the hazards associated with such lesions.

When penicillin became available for experimental purposes, we were given the opportunity to restudy certain phases of the intestinal obstruction problem. The factors of bacterial infection and toxemia in the pathogenesis of death from experimental obstruction, particularly, were reinvestigated.

It is the purpose of this report to summarize our studies on the effect of penicillin in experimental types of intestinal obstruction and to show why the conclusions reached demand new clinical emphasis on the phases of the problem which were investigated.

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PENICILLIN IN ISOLATED LOOP EXPERIMENTS

Prior to our experiments with penicillin in closed obstructed intestinal loops (12), it was known that animals with such lesions would die, usually within a week after the creation of the loops, in a manner which could best be explained on the basis of a toxemia. The pioneer studies of Stone, Bernheim, and Whipple had demonstrated that death in such experiments could not be explained on a basis of vomiting and that septicemia was not a factor. The numerous experiments to prove or disprove the elaboration of toxic substances within isolated loops have been critically reviewed by Cooper (1928), Morton (1929) and Besser (1940). Some investigators, notably Davis and Stone, Murphy and Brooks, Dragstedt, and Firor (10), believed that lethal toxins did develop in isolated loop experiments and furthermore that the source of these toxins was bacterial. This latter belief was based on a process of exclusion, as there was no positive way to rule out sources other than bacteria for the production of toxins.

In Dragstedt's experiments, the isolated loops were washed with ether. The dogs having washed loops survived much longer than did the controls. The possibility was never ruled out in his experiments that the ether might alter the loop mucosa, thus interfering with the absorption of toxins of any origin. Firor (10) demonstrated with U-shaped loops, having both ends open at the surface of the dog's abdominal wall so that periodic through-and-through cleansing with saline solution could be accomplished, that life was prolonged for considerable periods of time after the loops

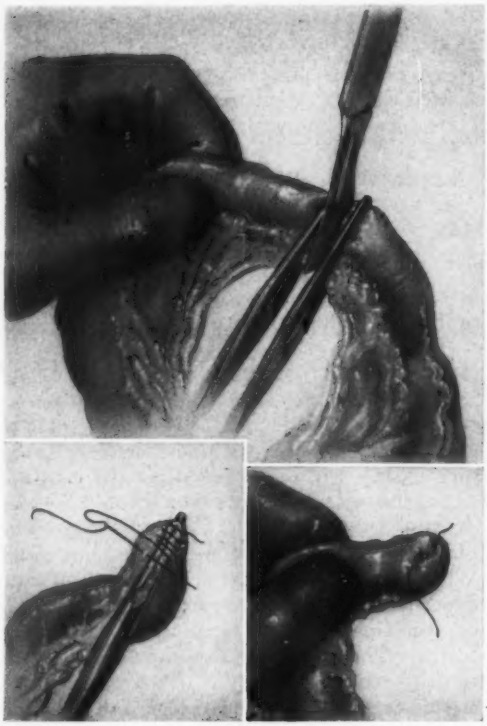

Fig. 1. Occlusion of bowel lumen by transection just above termination of antimesenteric artery of ileum and closure of proximal and distal ends.

were finally closed. The fact that in his experiments the animals eventually died of inanition obscured the mechanism of death in these experiments but again suggested the elaboration of lethal toxins of bacterial origin.

Firor's original suggestion (11) that a modern chemotherapeutic agent (sulfasuxidine) be employed in isolated loop experiments, was, I believe, the greatest contribution to the study of intestinal obstruction since the introduction of the Miller-Abbott tube by Abbott and Johnston. Firor and Poth (11) demonstrated that sulfasuxidine, when placed in closed, isolated loops, would protect animals with such obstructions for long periods of time. The work was confirmed (13). We had one such animal which was sacrificed over a year after operation. The objection to the sulfasuxidine experiments was that the mucosa was altered by being covered with a thick paste which could, theoretically, have interfered with the absorption of toxins of any origin. The observations of Firor and Poth led to the important studies of Sarnoff and Poth (18) and Sarnoff and Fine (19) who reported that sulfasuxidine had a protective effect in dogs with ileal lesions, produced by occlusion of the mesenteric veins, but in which the bowel lumen was unobstructed. Their studies established the important rôle played by bacteria in such lesions, but showed that sulfasuxidine must be present for some time for effective bacterial depopulation of the bowel to occur.

In 1945 it was shown (12), with the use of penicillin either placed in isolated loops or administered parenterally in dogs having isolated loops, that bacteria or bacterial products were responsible for the death of animals in such experiments. Furthermore, the lives of dogs having isolated obstructed jejunal loops could be prolonged for significant periods of time when penicillin was placed in the loops or was given intramuscularly. Thus, in 100 per cent of 15 control dogs with isolated jejunal loops, death occurred within 6½ days; 87 per cent died in 3½ days or less. In 100 per cent of 15 dogs, in whose isolated loops penicillin was placed, protection was afforded for 9 days; in 93 per cent for 13 days and in 60 per cent for over a month. One hundred per cent of 5 dogs treated parenterally with penicillin were protected for over 18 days. One dog lived over 2 months.

It was widely held at that time that penicillin was not effective against the gram negative bacilli. This study demonstrated that for all practical purposes, penicillin in large doses was effective *in vivo* against all the intestinal tract bacteria.

It was found that marked distention of the loop occurring in the presence of bacteriostatic agents was compatible with life. In the absence of distention of the loop, an abundant bacterial flora uninhibited by bacteriostatic agents was compatible with life. The experiments indicated that distention must be present before infection of the intestinal wall by the normal intestinal flora can occur. Microscopic and bacteriological evidence was presented to show that penicillin given prophy-

Fig. 2. Method of tying off mesenteric veins to ileal segment. a, Proximal turned in end; b, distal turned in end; c, rent in mesentery at distal extremity of segment to be strangulated. (Courtesy, *Bull. Johns Hopkins Hosp.*)

lactically in large doses, whether in a loop or parenterally, can prevent infection of the distended intestinal wall by the normal intestinal flora. Recently, in experiments employing streptomycin in rabbits with closed loops (created by tying off the base of the large appendix), a similar protective action was demonstrated (9).

PENICILLIN IN STRANGULATED LOW ILEAL OBSTRUCTION

In an attempt to produce an obstruction more like that occurring in man, and to test a treatment which might be effective for a similar type of obstruction in man, Dr. John D. Kennedy and the author (3) created strangulated low ileal obstruction in dogs by first completely occluding the bowel lumen (Fig. 1) and then tying off the mesenteric veins to a 60 centimeter segment of the obstructed bowel (Fig. 2). The resulting obstructions were characterized by severe strangulation (Fig. 3). The control dog's intestines all showed mucosal ulceration and massive bacterial invasion superimposed on the venous infarction which would often be accompanied by perforation. In the first 24 hours following the production of such lesions there would not always be peritonitis unless perforation had occurred. Later peritonitis developed whether or not there was perforation. The lesions in

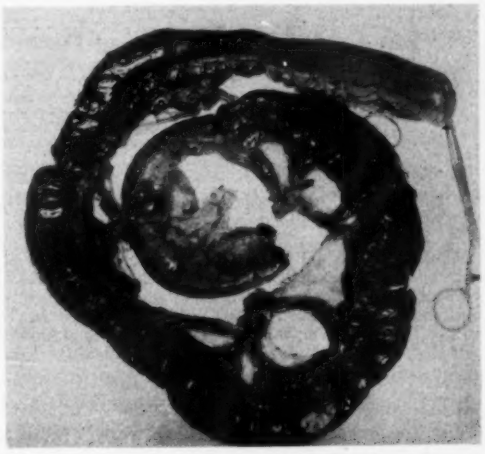

Fig. 3. Strangulated low ileal obstruction showing gross appearance of the resulting hemorrhagic infarction of the bowel wall. The proximal turned-in end is in center of photograph. In this particular case this lesion was resected 72 hours after its production in a dog treated with massive doses of penicillin. The animal was cured.

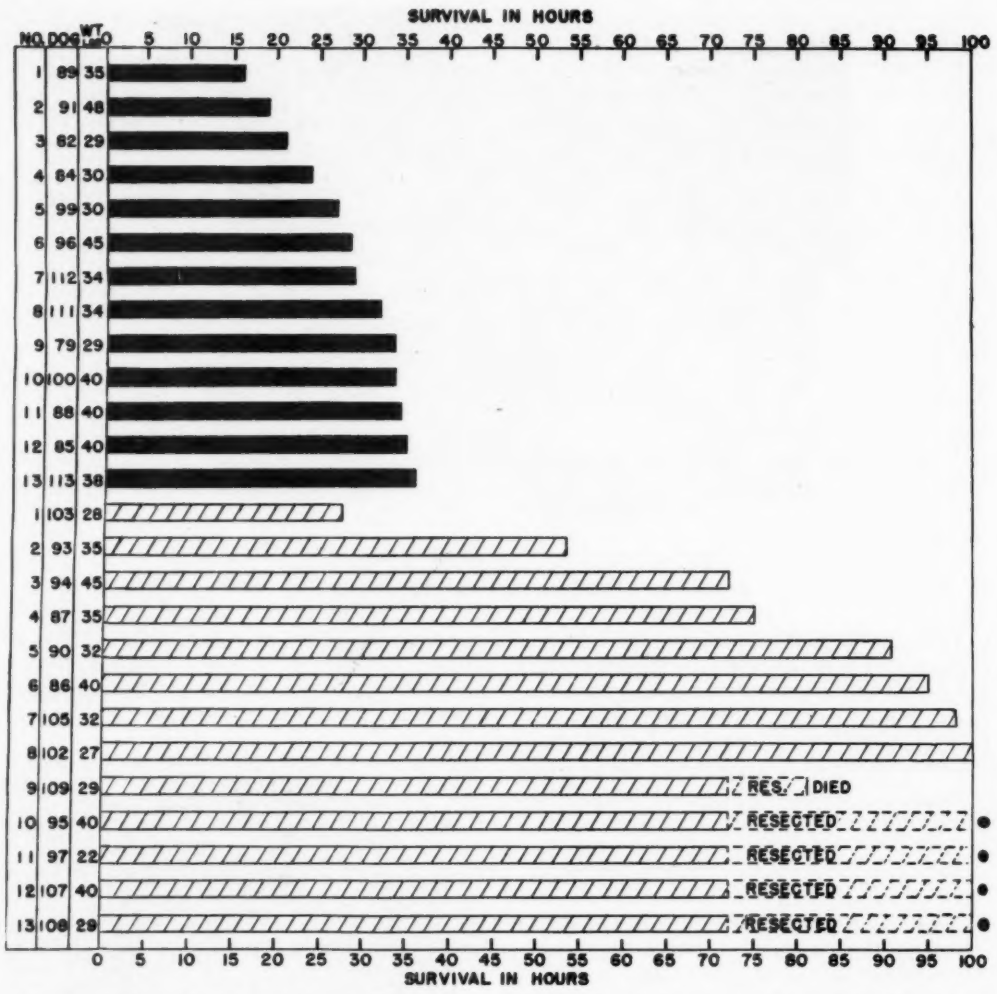

Chart 1. Diagram showing relative survival times of dogs with strangulated ileal obstructions not treated with penicillin as contrasted with the survival times of dogs with strangulated ileal obstructions treated with penicillin. It can be seen that 4 of the 5 penicillin treated dogs having late resections of their strangulated obstructions were cured. Both groups were treated equally for hemorrhage, shock, chloride, and water loss. Black, postoperative survival time of control dogs with strangulated ileal obstructions. Cross thatch, postoperative survival time of dogs with strangulated ileal obstructions, given massive doses of penicillin parenterally. Black dot, cures.

similar experimental obstructions which had been treated with massive doses of penicillin (100,000 units every 2 hours for 24 hours, 50,000 units every 2 hours during the next 48 hours, and 50,000 units every 4 hours during the remainder of the survival of these dogs whose weight averaged less than 16 kilograms) always showed a well marked bacterial invasion microscopically, but this was appreciably less than that which occurred in the controls.

Thirteen dogs, with this type of obstruction, treated with whole blood and gelatin solution intravenously and with physiological

saline solution subcutaneously to combat hemorrhage, shock, chloride and water loss, died within 36 hours. Seven dogs treated similarly, but with massive doses of penicillin in addition, survived between 50 and 100 hours (Chart 1). Six dogs lived 70 hours or longer; 4, 90 hours or longer. In addition, in 2 other penicillin treated dogs, resection of the strangulated obstructed bowel was performed at 72 hours (a period twice the survival of any control dog) with a cure in each animal. Later, in 3 more penicillin treated dogs, resections were carried out at 72 hours, with cure in 2 of the 3 dogs. Thus, there were 5 late resections performed at a time which was twice as long as any dog not treated with penicillin lived. Four of the dogs in which late resections were performed were cured. Drs. Robert J. Calihan and Henry N. Harkins aided us in these latter experiments and we reported the resection experiments with them (4).

In all cases, the control dogs and the dogs treated with penicillin were treated with equal vigor for shock, hemorrhage, chloride and water loss. In 2 of the penicillin treated dogs and 1 of the controls, volvulus of the strangulated bowel converted simple strangulated obstructions into strangulated closed loop obstructions. Thus it was demonstrated that penicillin, in the doses employed (which were massive) in the study, could prolong the lives of experimental animals having the type of strangulated obstruction chosen for the study. It was also demonstrated that this prolongation, though striking, was limited. Whether the limit was set by (1) the final inability of the penicillin, in the doses employed, to control bacterial infection, (2) fatal alterations in metabolic processes and body chemistry (the serum NPN, phosphorus and potassium were elevated, the sodium and chloride were normal to high and the carbon dioxide combining power was low), (3) the presence within the peritoneal cavity of necrotic strangulated bowel, or (4) some combination of these factors, could not be definitely established on the basis of this study. Because of the effect of penicillin in experiments with nonstrangulated closed loops, however, it would appear that the effect of penicillin would be much more striking in obstruction in which the degree or amount of strangulation was less marked.

These studies demonstrated that bacteria play an important rôle in the "toxemia" and death in dogs with strangulated ileal obstructions and that aggressive antibacterial therapy in the form of frequent, massive doses of penicillin is effective to a significant extent in treating such lesions.

THE FIELD FOR PENICILLIN THERAPY IN HUMAN INTESTINAL OBSTRUCTION

In a study of 204 cases of acute, complete, mechanical obstruction of the small bowel, in which patients were operated upon at the Johns Hopkins Hospital during the 10-year period, 1936–1945, there was an overall mortality of 20 per cent (5). When this mortality rate was corrected for deaths due to cardiac, pulmonary, and other causes not directly related to the intestinal obstruction, the mortality rate was 15 per cent. Of the 41 deaths in the series, over half were due to peritonitis. In 27 per cent of all cases, the bowel was strangulated at operation. In an additional 5 cases, although the bowel was considered viable by the surgeon at operation, gangrene and necrosis were found at autopsy. The strangulated cases accounted for over half of all the deaths due to peritonitis. The study confirmed the statement of McKittrick and Sarris that "the factor of strangulation is the greatest single factor determining the outcome of a case of intestinal obstruction," and showed that there is a fertile field for an adjunct against bacterial infection in intestinal obstruction. Indeed, it would seem that no further great reduction in the present mortality rate can be made until bacterial infection and "toxemia" are combated.

DISCUSSION

Evidence has been presented which demonstrates the important rôle played by bacteria in death resulting from the types of obstruction studied. Furthermore, it has been shown that the lethal effects of bacterial growth can be significantly obviated by massive doses of penicillin. It should be stated here that the exact mechanism by which bacteria produced their lethal effects in our experiments is not

clear. We feel that the ascribing of all deaths in experiments of this nature to peritonitis is an over-simplification of the problem (14). At any rate, it would seem that the beneficial results of penicillin therapy, noted in our experimental animals, could be applied directly to man. Human studies have revealed that the problems of strangulation and infection are grave ones; and also that the presence of strangulation is often impossible to diagnose, especially in patients with early cases, short of direct visualization of the affected bowel wall.

When these factors are combated in experimental animals, life is prolonged and significant protection is afforded.

CONCLUSIONS

1. A clinical trial of massive antibacterial therapy for acute mechanical small bowel obstruction in man is warranted.

2. It is believed that such a trial would significantly lower the present intestinal obstruction mortality.

3. Penicillin should be regarded as an adjunct to early and adequate surgical intervention in acute obstruction, and not as a means to delay operation.

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MAJOR AMPUTATIONS

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THE changes which have come about in the surgical treatment of amputations due to the recent war effort and which are adaptable to use in civilian life have been chiefly the result of good planning and organization for the care of these cases. The early establishment of the use of sound surgical principles and practices for the early and immediate care and transportation of war amputations and implementation of these policies by authoritative directives was an important part of this planning. This together with the establishment and organization of special centers for definitive care and rehabilitation contributed more than anything else to whatever changes for the better there may have been in surgical treatment. The modern advances in medicine, medical education and graduate education played the rôle of making a higher standard of practice of medicine and surgery available, but all these would have amounted to very little had it not been for proper organization (5). This brought the patients together under the direction of highly specialized surgeons who had the responsibility for not only organizing the whole functioning of the center with all its different departments but for all of the complete care of the whole patient and all of his problems. Even here in the amputation centers the value of organization could hardly be overestimated. For truly surgery is not the end but one of many means to the end in this field. Besides organization, it was chiefly due to the fact that the surgeons were in complete charge of all of the amputee's problems from the time of his amputation until he was fitted with a limb and trained to use it, that better surgery was done with better results than ever before (1).

These are the important lessons learned from the War and herein lie the hints for the wise if service is to be improved for civilians in the future. It is, of course, impossible and unnecessary to duplicate the war services in civil life, but it would be a simple matter indeed to establish organized amputation services in the larger civilian hospitals, just as fracture and other special services were developed in the past. The management of amputations would then improve just as fracture treatment has. There is no obvious reason why existing limb makers could not co-operate completely with the surgeons in this matter just as brace makers always have. There can be no quarrel between surgeons and limb makers. The ultimate aim of both should be to give the patient the best possible care. If either or both fail in this important task they may find someone else doing their work for them. For if something is not done to improve the care of civilian amputees the federal agencies may justifiably take over the whole problem including especially the manufacture and fitting of artificial limbs.

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SURGERY

The strongest trend in the surgery of amputations has been toward more conservatism. This has been true both in the immediate surgical treatment and in the definitive surgery. The general use of the modified guillotine amputation at the lowest possible level resulted in the saving of more of the limb than ever before in war or civil life, both at the time of primary amputation and finally when definitive surgery was done. The more complete understanding of the problem of the amputation stump in its relation to the prosthesis by the surgeons has resulted in a more conservative surgical attitude with a marked tendency to leave as much stump length as possible and to fit the remaining stump with a prosthesis regardless of its length. The chief exception to this is amputations below the knee of more than 7 inches in length. One of the truly great lessons learned was that the problems of the surgery of the stump are so closely related to those of the prosthesis that it is impossible to completely understand one without under-

standing the other, and that they cannot be separated from one another. Since the surgeon is the only one who can understand all of the problems, particularly these two, he is the only one who is or ever will be qualified to properly supervise and direct the whole care of the amputation stump and the patient.

The important changes that have come about in the surgical treatment of amputations, then, have not been due to the development of new operations, techniques, or methods. Rather they are due to organization, good judgment, good surgery, and, most important, the complete responsibility of surgeons for the whole patient and all of his problems. The problem is an arduous one and nothing has been found which will take the place of hard work and the greatest attention to details.

1. The open or modified guillotine amputation. The routine use of this method of amputation in the United States Army has again proved to be the safest and best method for use in war, notwithstanding some opinions to the contrary. Although long skin flaps which tend to close the wound prematurely are undesirable, it is important that viable skin be conserved at least equal in length to the bone. The use of the modified guillotine amputation at the lowest level consistent with proper débridement without regard to the final site of amputation, with proper skin traction until the stump is ready for final revision or reamputation, has proved to be of such great value in the war that it must find greater use in contaminated civilian cases. The stump is ready for revision or reamputation in from 3 to 8 weeks postoperatively, depending upon the case. Reamputation at a higher level, when indicated, can be done much earlier than revision at or near the stump end. This is one of the reasons why the original open amputation should be done at the lowest possible level. The stump is ready for revision when the skin has been pulled well down over the stump end, drainage has ceased, swelling has subsided, and the remaining open wound is clean. Routine bacteriological examination of the stump wound is advisable before the final operation is done. It is not necessary or desirable in the majority of cases to wait for complete healing to take place (6).

The use of skin grafts on amputation stumps is mentioned only to be condemned. They are distinctly disadvantageous in that they stop the whole normal healing process and they are poor substitutes for the normal skin which can easily be drawn down over the stump-end by traction. When skin grafts are used they interfere with the function of the stump in the prosthesis by breaking down to such an extent that they should routinely be removed and traction applied until the skin can be closed. The removal of skin grafts from stumps for use elsewhere is equally to be condemned as the donor area causes difficulty when the prosthesis is applied.

2. Essential points in amputation. (a) The operation should be done with the use of a tourniquet whenever possible. The use of the tourniquet can be extended by the use of Wyeth pins on short thigh stumps.

b. Definitive operation should be done in a clean field and under careful aseptic precautions.

c. Except in end-bearing stumps, the skin flaps should be cut equal in length so that they meet in the center of the end of the stump, without redundancy. A general rule for estimation of the length of the skin flaps is to cut each flap approximately two-thirds of the length of the radius of the limb. The stretching of the flaps, which then results after undercutting, permits them to lengthen sufficiently for closure.

d. The deep layer of fascia is reflected with the skin flap in primary amputation whenever possible. The muscles are divided slightly distal to the saw line, so that after retraction has taken place the end of the muscles will be at the level of bone section.

e. The periosteum is sharply divided at the level of bone section.

f. The main nerves are gently pulled down, smoothly divided, and allowed to retract out of the stump end. Nerves are not ligated, cauterized, injected, or otherwise treated by any fancy technique.

g. The tourniquet should be removed after the main vessels have been ligated and complete hemostasis obtained. The skin flaps are closed by simple interrupted skin sutures. The use of subcutaneous and stay sutures is not

only unnecessary but contraindicated in that they further traumatize already ischemic flaps.

h. Drainage should be used more or less routinely for 24 to 48 hours in all amputation stumps because of the tendency for postoperative drainage from the mass of sectioned muscle and from the bone.

3. Postoperative care. There is no substitute for complete bed rest, elevation and proper splinting in amputations below the knee, until complete wound healing has taken place. A period of at least 3 to 4 weeks is required for proper healing of these cases. Other amputations may heal in less time. Postoperative splinting is preferable to skin traction even in cases in which the skin flaps are tight. Amputations through, or above, the knee should not be elevated as this causes flexion contractures. These patients, particularly bilateral above the knee amputees, should be turned face down at intervals whenever possible to prevent contractures. The routine use of elastic bandages for compression dressings has been found to be of great value.

Exercises designed to overcome contractures, and to strengthen the muscles of the stump, are started as soon after wound healing as possible. Wrapping of the stump with elastic bandages for stump shrinkage, when properly carried out, has proved to be of great value. Exercises and wrapping are the only two forms of physiotherapy which are of value. Massage is always contraindicated as it may be harmful and is of no value.

Occupational therapy has proved to be important, both in keeping the patient's mind occupied while he is waiting, and also in the training of the use of the arm prosthesis.

4. Extension grafts. The extension of the bone length of certain stumps when the normal soft tissues were present but were devoid of a considerable length of bone proved to be a practical and valuable procedure in certain cases, particularly in amputations above the elbow. The fibula has been successfully used as an intramedullary extension graft in the medullary canal of the humerus.

The use of extension bone grafts on amputation stumps where any type of skin graft is required to extend the length of the stump is probably not justified in most cases in view of the disappointing results obtained. This is true of arm stumps as well as various types of amputations of the hand, thumb, and fingers.

5. Homogenous bone and bone bank. The successful use of freshly transplanted homologous bone grafts in a number of patients with multiple injuries and amputations who had no bone graft donor site led to the limited use of a bone bank at the Thomas M. England General Hospital. The bone was collected from clean reamputations and stored in an ordinary electric refrigerator in glass jars containing normal saline solution saturated with sulfanilamide. The use of bone preserved in this manner was not great enough to warrant conclusions as to its value, but the experience was sufficient to suggest further experimentation with the method. This experience did prove beyond doubt that freshly transplanted homologous bone gave good final end results in a high percentage of the cases. These results will be published in a subsequent paper.

6. Sulfa drugs and penicillin. The use of medication of this type has undoubtedly been helpful in combating serious infections and has saved time in some cases. The routine preoperative and postoperative use of medication of this type, however, has not been proved to be of outstanding value.

SITES OF MAJOR AMPUTATIONS

1. Amputation of all digits at or near the metacarpophalangeal joints. Phalangization of the metacarpals, with complete removal of the second and third and sometimes the fourth metacarpal bones, and plastic closure of the remaining defect, with the formation of a deep cleft, was found to be the best solution to this problem type of amputation. The remaining digits thus formed have the advantage of sensation, active motion, and prehension. They were so capable of function that all patients operated upon were completely satisfied with the results. The function thus obtained is in some ways similar to that of a Krukenberg stump. This type of stump is very satisfactorily fitted with a cosmetic hand which is used on occasions when active function of the stump is secondary to cosmetic appearance. The technique of this procedure will be described fully in a subsequent article.

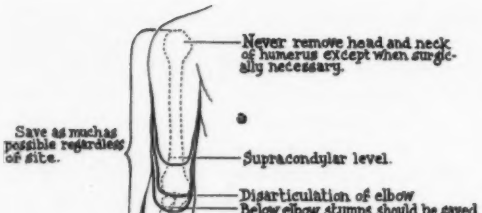
Never remove head and neck of humerus except when surgically necessary.
Save as much as possible regardless of site.
Supracondylar level.
Disarticulation of elbow
Below elbow stumps should be saved regardless of length, when possible.
Junction of lower and mid-third.
Disarticulation of wrist.

Fig. 1. Sites of major amputations in upper extremity.

2. Amputation at the wrist joint. Amputation at the wrist joint has been revived, both in this country and in Europe. The carpal bones should be conserved if possible, but if not, disarticulation without them is satisfactory. Amputation at this site conserves length and when properly fitted with a prosthesis there is some useful pronation and supination. The prosthesis does not extend above the elbow. Amputation at the wrist is somewhat more difficult to fit with a prosthesis than amputation at the junction of the lower and middle third of the forearm, but this can usually be overcome by effort and experience. There have already been many improvements in the prosthesis for amputations at the wrist both here and in England (4).

3. Amputation at the junction of the lower and middle third of the forearm. If amputation through the wrist is impossible, the next level of choice is at this level, or approximately 2 inches above the styloid process. Before the war this was the standard site of amputation in the forearm, and was preferred by most surgeons and limb fitters. All possible length should be saved above this level.

4. Short below elbow stumps. All length possible should be saved below the elbow since improved methods of fitting have resulted in greater ability to fit these short stumps than ever before. It is possible to fit satisfactorily below the elbow stumps as short as one-half inch in length. The relative stump length may be slightly increased by resection of the biceps tendon at the time of final operation. This can easily be done by reflecting the anterior flap without the necessity of making a separate incision (3a).

5. Disarticulation of the elbow. Amputation at this level was found to be more useful than it had previously been thought to be. It is preferred to amputation at the supracondylar level wherever possible as it gives the stump longer leverage and when properly fitted the patient has better control of the prosthesis, particularly in performing internal and external rotation movements. The prosthesis is fitted with side joints and the type of prosthesis is similar in principle to that used for end-bearing thigh stumps.

6. Amputations at the supra-condylar level. This is still the standard site of amputation above the elbow. The supracondylar amputation should be left as long as possible. The site of bone section is immediately above the condyles of the humerus. Above this level all possible stump length should be saved.

7. Short above elbow stumps. A stump at least 2 inches in length below the axillary fold is necessary for the active use of a prosthesis. If the stump is shorter, all possible bone should be saved, including the head and neck of the humerus, despite the fact that amputations at this level will be fitted as disarticulations of the shoulder. Attempts to increase the relative length by section of muscles and tendons have proved disappointing.

8. Disarticulation of the shoulder. Disarticulation of the shoulder should never be performed except where surgically necessary. The head and neck of the humerus should be conserved wherever possible for contour and normal appearance. This surgical conservatism also results in better prosthetic fitting and improved prosthetic accomplishment.

SPECIAL METHODS FOR USE IN UPPER EXTREMITY[1]

The Krukenberg operation (or stump). The Krukenberg method consists of surgical separation and phalangization of the radius and

[1]The basis for the statements used in connection with the Krukenberg and cineplastic methods was personal observation in the American Occupied Zone in Germany when the author was a member of the Army Surgeon General's European Commission on Amputations and Artificial Limbs (1946).

ulna so that the resulting claw shaped stump is capable of some prehension and has the advantage of sensation. The use of this procedure is limited to amputations below the elbow of at least 11 centimeters in length from the lateral epicondyle. Although the method has been widely used in Germany, particularly on bilateral amputees, with or without eyesight, it probably would not meet with general acceptance in this country. The use of the Krukenberg method, however, should be valuable in the surgical treatment and rehabilitation of all blind bilateral amputees.

The cineplastic method. The only form of cineplasty still in use is the muscle tunnel type of Sauerbruch. It is still widely used by some surgeons in Germany, and the surgical technique has recently been improved considerably. The use of this method has been limited in this country and discontinued in most others chiefly because of inadequate prosthetic facilities. There has recently been considerable renewed interest in cineplasty, but extensive use of the method must await further prosthetic research and development which is being carried on by the Committee on Artificial Limbs of the National Research Council. When this work has been completed, the method may well be subjected to more extensive trial use when its true value in this country can be finally determined.

LOWER EXTREMITY

1. *Amputations through the foot.* Partial amputations of the foot up to the Chopart level can usually be fitted with shoe corrections and appliances so that they will give very satisfactory function. One of the important lessons learned in the recent War was that the Chopart amputation could not usually be fitted with anything in the way of a shoe correction or a prosthesis which was satisfactory. The Syme amputation is therefore almost always preferable to the Chopart. Much time, worry and dissatisfaction can be prevented on the part of the patient and surgeon by the early and immediate application of the Syme amputation to almost all of these cases. Attempts to improve the function of the Chopart amputation by subastragalar and ankle joint fusion have usually been unsuccessful.

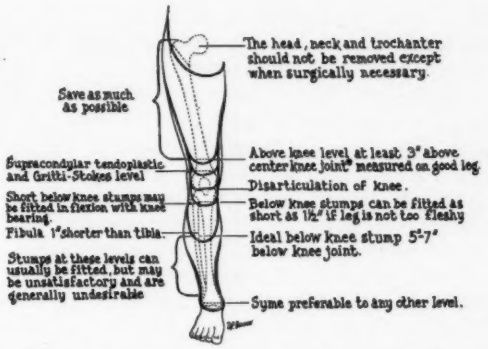
The head, neck and trochanter should not be removed except when surgically necessary.
Save as much as possible
Supracondylar tendoplastic and Gritti-Stokes level
Above knee level at least 3" above center knee joint* measured on good leg
Disarticulation of knee.
Short below knee stumps may be fitted in flexion with knee bearing.
Below knee stumps can be fitted as short as 1½" if leg is not too fleshy
Fibula 1" shorter than tibia
Ideal below knee stump 5"-7" below knee joint.
Stumps at these levels can usually be fitted, but may be unsatisfactory and are generally undesirable
Syme preferable to any other level.

Fig. 2. Sites of major amputations in lower extremity.

*Center of knee joint is the center of axial motion which is located in the center of the femoral condyle, ¾ inch above the joint line.

2. *The Syme amputation.* The Syme amputation, when properly performed under the proper circumstances, is preferable to any other major amputation in the lower extremity. It is the only amputation recommended at the ankle. The use of amputation at the ankle was greatly revived in this country during the recent war, although it had previously been used only to be generally forgotten. Details concerning the Syme amputation during the War have been published in two previous articles (2, 3).

3. *Amputations below the knee.* Although amputations in the lower third of the leg, above the Syme level, may be satisfactory in some cases, they are not generally favored, because of poor circulation. The ideal level of amputation below the knee is generally accepted to be five to seven inches below the knee joint. Most surgeons, who have had the greatest experience, prefer a length of not over 5 to 5½ inches below the knee joint. The use of partial or complete ischial weight bearing has been found to be useful in fitting many imperfect below the knee stumps.

4. *Short below the knee stumps.* The fibula should be completely removed in all below the knee stumps shorter than 3½ inches, and these may be fitted as short as 1½ inches below the knee joint if the leg is not too fleshy. Success in fitting these short stumps depends upon the proportion of length to width. Stumps with little soft tissue covering, there-

fore, are more favorable at this level. Some of these short stumps are advantageously fitted with considerable end weight bearing. Section of the hamstring tendons may give additional relative length to the stump in some cases (3a).

5. *The flexed leg stump (bent knee).* Below the knee stumps, which have for any reason definitely proved to be unsatisfactory, or are too short for fitting as below knee stumps, may be flexed to 90 degrees and fitted very satisfactorily with a prosthesis with full weight bearing on the bent knee. If sufficient stump length projects posteriorly in this type of fitting, it has the advantage of full end-bearing, without the necessity of any type of belt or suspenders for suspension of the limb. This is one of the oldest methods of prosthetic fitting in the lower extremity, the use of which has been revived in the War.

6. *Disarticulation of the knee.* Amputations at this site may give excellent results in some cases. It is important that the greatest care be exercised in performing amputations at this level. Unless good healing and full end-bearing are obtained, the results may be disappointing.

The patella is left in position without removal of the cartilage unless more length is desired in the anterior flap. Removal of the patella in such cases may result in considerable additional relative length of the anterior flap. The cartilage of the femoral condyles is not removed. It is important that the hamstring muscles be sutured to the patella tendon in the intercondylar notch to prevent separation of the skin flaps. When properly fitted with a prosthesis, most of these cases need no pelvic or shoulder suspension of the limb, since accurate fitting of the socket to the bulbous end of the stump secures it in place.

7. *Supracondylar amputation of the thigh.* The supracondylar tendoplastic amputation apparently gives equally as good results as the Gritti-Stokes. The only difference in these two amputations is that the patella is excised in the supracondylar tendoplastic procedure, whereas it is fixed to the end of the femur in the Gritti-Stokes. The supracondylar tendoplastic amputation has the advantage of being a simpler surgical procedure than the Gritti-Stokes. The former was more commonly used in the Army amputation centers than the latter.

8. *Amputations above the knee.* In amputations above the supracondylar Gritti-Stokes level, the end of the stump should not be longer than 3 inches above the center of the knee joint.[1] Many surgeons of great experience prefer an ideal length of not over ten to twelve inches from the trochanter. If amputations of the thigh are longer than 3 inches above the center of the knee joint, it will be necessary for the prosthetic maker to make the thigh piece longer than the normal thigh, and the shin piece shorter than normal so that the knee joint of the artificial limb can be incorporated. All possible length should be saved above this level.

9. *Short above the knee stumps.* It is possible for above the knee stumps as short as 2 inches, measured from the crotch, to be fitted as above the knee amputations. Here again this depends somewhat on the proportion of length to width, the thinner ones being preferable. If a short thigh stump proves to be too short to be fitted as an above the knee amputation it may be fitted with a tilting table as a hip joint disarticulation when the stump is flexed to 90 degrees. The head, neck, and trochanter should never be removed except when absolutely necessary, as the presence of this structure helps to stabilize the prosthesis and it conserves the normal contour of the pelvis.

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[1]Center of the knee joint is the center of axial motion, which is located in the center of the condyle of the femur about three-fourths inch above the knee joint.

ADVANCES IN BONE GRAFT SURGERY ATTRIBUTED TO WORLD WAR II

GEORGE K. CARPENTER, M.D., F.A.C.S., Nashville, Tennessee

BONE graft surgery as performed by the military surgeons during the early months of World War II was little different from that performed in civilian life. Sound civilian surgery became good military surgery. The advances derived from war experience should now be applied to present day civilian practice.

Experience has shown that better end-results are obtained when both the patient as a whole and his extremity are effectively prepared for bone graft surgery. The patient's general condition should be at its best prior to surgery. Blood transfusions are often indispensable in rendering the patient in optimum condition for surgery. It has been well shown by Brown, Shaw, Mech and others that existing scar tissue must be appropriately treated prior to bone graft surgery. Once nonunion is accepted, the extremity is subjected to a well supervised preoperative program of physical therapy which is outlined to improve circulation and muscle tone and to mobilize the joints.

Presented in the symposium on Fractures and other Trauma before the Clinical Congress of the American College of Surgeons Cleveland, Ohio, December 16–20, 1946.

Chemotherapy plays an important rôle in bone graft surgery. This is particularly true since nonunion so frequently follows a compound fracture. Chemotherapy will not permit bone graft surgery in the presence of infection. It is our practice to delay bone graft surgery until approximately 3 months following complete wound healing. The time interval between complete wound healing and bone grafting may vary somewhat, depending upon the character and duration of the infection, but it is safer for the patient if the surgeon waits longer than was necessary, rather than to operate too early. It is our practice to employ adequate penicillin therapy for 2 days prior to surgery and for approximately 5 days following surgery.

It is believed that nonunion is too often not recognized and accepted in an early stage, and as a consequence, bone grafting is frequently unnecessarily delayed. So called delayed union usually progresses to nonunion. To treat delayed union for 3 months and at the end of this time find that bone graft surgery is necessary, is most time-consuming to the patient. Prolonged immobilization is detrimental to restoration of function. The morbidity of a

Fig. 1. Fig. 2.

Fig. 1. Case 1. Nonunion of 6½ years' duration in an 8 year old child.
Fig. 2. Case 1. Three and a half months after bone graft with iliac bone.

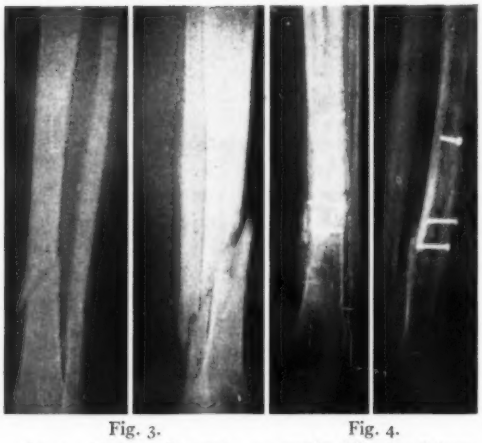


Fig. 3. Fig. 4.

Fig. 3. Case 2. Nonunion 2 months following injury.
Fig. 4. Case 2. Three months following sliding inlay bone graft.

fracture is in direct proportion to the extent and duration of the disability and its associated economic sequelae.

In cases in which the surgeon is reasonably assured that nonunion is inevitable, bone grafting should not be delayed except as is necessary to fulfill the usual prerequisites for bone graft surgery. Unless the surgeon is reasonably assured that so called delayed union will soon progress to solid bone union, it is believed that bone grafting should be performed without delay. Carpenter,

Fig. 5. Fig. 6.

Fig. 5. Case 3. Nonunion 5 months following severe compound fracture.
Fig. 6. Case 3. Two months following onlay graft.

Rosenfeld and Mech have described the treatment of limited union by reinforcement bone grafts as a procedure planned to shorten the time needed to obtain a bony union of sufficient size and strength to permit early and unprotected function of the extremity. This treatment of limited union decreases the disability, and thereby reduces the morbidity of the fracture.

A patient with nonunion requires a careful consideration of the individual problem at hand, and a method of procedure is planned which will assure the maximum of function in the minimum of time. Needless to state, the

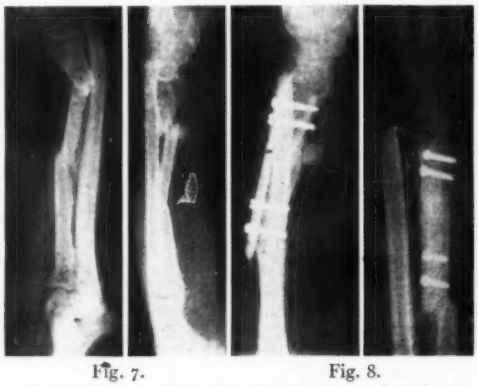


Fig. 7. Fig. 8.

Fig. 7. Case 4. Nonunion of radius 6 months following severe compound fracture. Healing complete for 3 months.
Fig. 8. Case 4. Roentgenograms showing union 7 weeks after onlay graft.

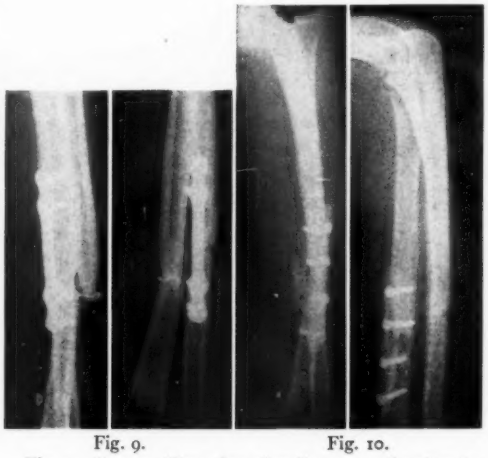


Fig. 9. Fig. 10.

Fig. 9. Case 5. Nonunion of radius 4 months after injury.
Fig. 10. Case 5. Roentgenograms 6 weeks after onlay graft.

procedure of choice must be a safe one for the patient, and this will necessitate sound surgical judgment and respectful understanding of morbidity. Cancellous bone, such as that obtained from the wing of the ilium, offers exceptional qualifications as the graft of choice. It is ideal for a spinal or sacroiliac fusion and in nearly all joint fusions which necessitate the use of autogenous bone. Unfortunately, the usual bone graft operation for nonunion is performed with the patient on his back, and since the posterior wing of the ilium presents the better donor site, certain technical difficulties most often make the ilium an impractical site from which to obtain the grafts. Adequate internal fixation of the fracture site is very advantageous and can be better obtained by the application of an onlay graft with screw fixation. Cancellous bone in lesser quantities can, of course, be obtained from the tibia. The tibia serves as the best donor site in the majority of cases. Multiple chip grafts, as can be obtained from the tibia, also serve to stimulate osteogenisis.

The long bones may be better grafted by the application of long tibial grafts with cancellous bone and chips packed about the fracture site and along the graft. Two to four screws will, as a rule, adequately maintain internal fixation of the fracture and graft. Frequently, in nonunion of the femur, the fracture is fixed by the application of a six screw metallic plate to facilitate postoperative treatment in a Thomas splint and a Pearson attachment traction apparatus. Nonunion of the femur thus treated by the application of a metallic plate in addition to a tibial graft and cancellous bone eliminates the use of plaster and permits early knee motion. Although it is believed that positive fixation of the fracture and of the graft very materially hastens the union, such treatment is not always employed.

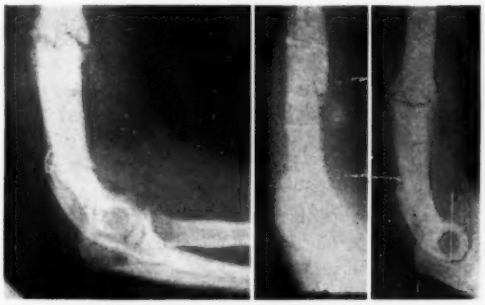


Fig. 11. Fig. 12.

Fig. 11. Case 6. Nonunion of humerus 4 months after severe compound fracture. Wound healing complete for 3 months.

Fig. 12. Case 6. Roentgenograms 8 weeks after onlay graft.

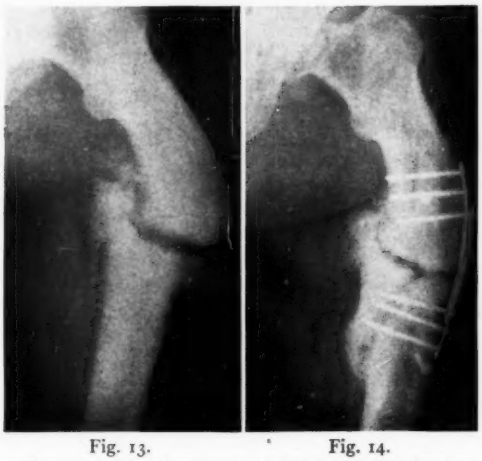
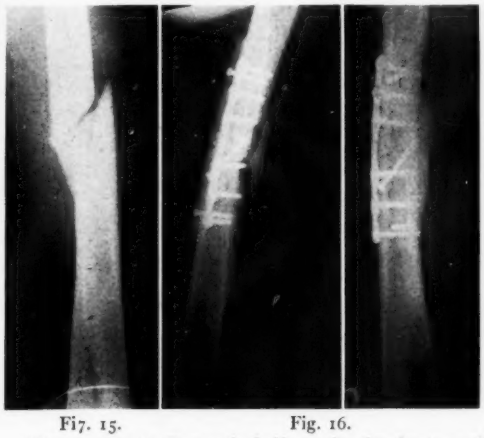


Fig. 13. Fig. 14.

Fig. 13. Case 7. Seven and a half months after fracture of femur.

Fig. 14. Case 7. Seven months after application of onlay graft and plates.



Fi7. 15. Fig. 16.

Fig. 15. Case 8. Two and a half months after fracture of femur.

Figs. 16 and 17. Case 8 Five months after onlay graft and plate.

As a general rule, plates and screws are used sparingly, if at all, in treating a case of nonunion which previously showed infection, even though wound healing had been complete for at least 3 months. Bones well covered with muscles, such as the shaft of the humerus and femur, will tolerate plates and screws much better than such locations as the lower third of the tibia. The site of the nonunion should be cleared of scar tissue and sclerotic bone, but when extensive infection has been present, it may be unwise to treat the fracture site. An onlay graft may be reasonably expected to take without performing an extensive resection of scar tissue and sclerotic bone. A sliding inlay graft is an excellent procedure for treatment of nonunion of the tibia following a simple fracture, but when nonunion follows a compound fracture of the lower third of the shaft of the tibia, an onlay graft, without screw fixation, is applied to the lateral aspect of the tibia. Intermedullary grafts are rarely, if ever, used. With loss of substance, multiple grafts with much cancellous bone and chips are employed in an effort to restore the bone to its normal size. It is imperative that plenty of bone be used in every case. The surgeon must be ingenious and resourceful and an exponent of sound surgical principles.

SUMMARY

The advances in bone graft surgery emanating from the experiences of World War II, which are equally applicable to civilian practice, are briefly as follows:

1. A full appreciation of the value of rendering the patient in optimum condition for surgery and maintaining his blood and nutritional requirements throughout the convalescense, as so well described by Lyons.

2. Like the patient as a whole, the extremity itself is likewise put in optimum condition for surgery.

3. Chemotherapy will permit the infected compound fracture with nonunion to be grafted earlier, but never until the elapse of an adequate time interval following complete wound healing.

4. An early recognition of nonunion will permit grafting as soon as the usual prerequisites for bone graft surgery are satisfied.

5. Adequate internal fixation of the fracture and of the graft, preferably by using screws and a tibial graft, seems to stimulate the osteogenetic activities of the graft and is desirable except when the site of fracture was previously the seat of an extensive infection.

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FRACTURE OF THE CARPAL SCAPHOID

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THE navicular of the hand is invariably called the scaphoid by those who write of its pathologic state. Obletz and Halbstein (1) described the nutrient foramina on which the blood supply of this bone depends. The largest and most numerous of these foramina are distal to the constricted portion called the "waist" by clinicians. These writers concluded that a complete fracture at the waist would seriously interfere with the blood supply of the proximal fragment in about a third of the cases. *This is the important factor in the healing of these fractures.*

Mechanism. These fractures are due to indirect violence transmitted from the outstretched hand along the radial axis of the hand and forearm. These radial axis injuries are in order of sequence but not frequency as follows: (1) fracture of the first metacarpal bone, (2) fracture of the greater multiangular bone, (3) fracture of the carpal scaphoid, (4) perilunate posterior dislocation of the carpus, (5) Colles' fracture, (6) fracture of the head of the radius. These lesions occur separately and in combination (Fig. 1 and Fig. 2). In the younger age group, such as we had to deal with in the armed forces, whose strong muscles resist the indirect violence, fracture of the carpal scaphoid occurs 4 to 5 times as frequently as Colles' fracture. In the more elderly with flabby muscles, the wrist immediately extends and Colles' fractures predominate.

Clinical recognition of the fracture. If, after a fall on the outstretched hand or similar trauma, the patient complains of pain at the radial side of the carpus, inability to grasp firmly, and shows no obvious deformity but constant, definite tenderness in the interval between the long and short extensor tendons of the thumb, a fracture of the carpal scaphoid should be assumed to exist until its absence is proved by roentgenogram.

Presented in the symposium on Fractures before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–20, 1946.

Roentgenography. The use of the roentgenogram as an aid to diagnosis in a very high percentage of wrist injuries led to the discovery of an enormous number of these carpal scaphoid fractures in the armed forces. A complete or widely displaced fracture may be immediately revealed by the first roentgenogram in conventional positions. At times the first roentgenogram will fail to reveal the fracture, which will be readily seen 2 weeks later due to absorption at the fracture line. Those views which show this fracture to best advantage are (1) an anteroposterior with the hand in marked ulnar deviation, and (2) a posteroanterior in 45 degree angle oblique projection.

The fracture. A few of these fractures occur at the tuberosity where the transverse carpal ligament is attached. These avulsion fractures heal uneventfully in short order.

The fracture under consideration occurs at the waist and heals according to the blood supply which remains to the proximal fragment. Fractures with an adequate blood supply to the proximal fragment should heal with 8 to 10 weeks of immobilization, while those with an

a b

Fig. 1. Cpl. S.F. Jeep accident December 16, 1945, Korea. Plaster splint was applied immediately. a, Earliest roentgenogram available March 15, 1946, shows healed fracture of left first metacarpal bone; fracture of left carpal scaphoid unhealed. b, Roentgenogram 3 months later, June 13, 1946, carpal scaphoid healed. This case illustrates a combination of two radial axis injuries.

Fig. 2a.

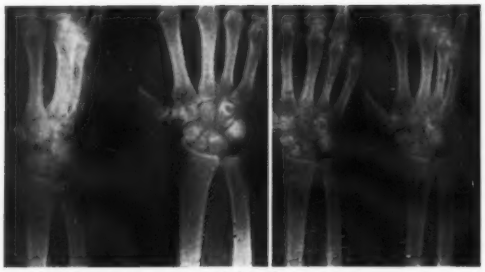

Fig. 2b.

Fig. 2. Pvt. H.L.B. Jeep accident November 16, 1945, France. Injuries recognized and treated immediately. a, at left, Roentgenogram of right wrist showing a perilunate dislocation with a complete badly separated fracture of the scaphoid. a, at right, Roentgenogram of left wrist on day of injury showing fractures of greater multiangular, carpal scaphoid and Colles. b, at left, Roentgenogram of right wrist July 30, 1946, 8 months after injury. Dislocation reduced, scaphoid fracture ununited. a, at right, Roentgenogram of left wrist July 30, 1946, 8 months after injury. Fracture of greater multiangular and Colles are united. Carpal scaphoid ununited. This case is shown as a bilateral carpal scaphoid fracture with three other associated radial axis injuries in the two wrists. This soldier refused further treatment, stated that his symptoms were minimal. He could do his civilian job and requested discharge from the service.

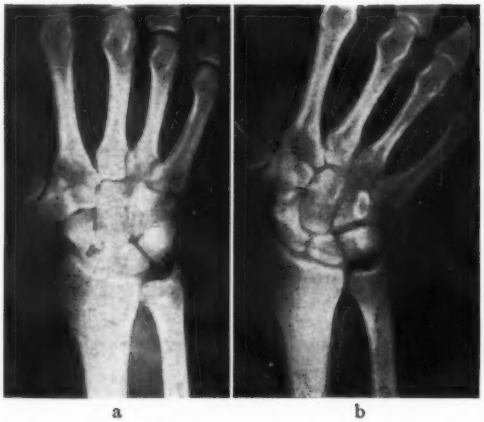

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Fig. 3. Cpl. E.M. June 2, 1945, France. Fall on outstretched right hand. Treated 3 months as a *sprain of wrist*. a, Roentgenogram November 3, 1945, 5 months after injury showing fracture of right carpal scaphoid with marked absorption at fracture line. b, Roentgenogram, July 3, 1946, 13 months after injury, shows carpal scaphoid fracture healed. This soldier was disabled 13 months, at least 8 months longer than necessary because his injury was unrecognized.

inadequate blood supply will require up to 20 weeks or longer before healing ensues. Unfortunately, there is no means of determining in advance into which group any given fracture of the scaphoid falls.

TREATMENT

Treatment of the fracture is by prompt immobilization of the wrist in a glove type circular plaster splint extending from just below the elbow to the distal palmar flexion crease, allowing full motion in the fingers. The wrist is in slight dorsal flexion. The thumb is usually immobilized in anatomic position beyond the distal joint. Various positions of the thumb have been advocated with equally good results reported. This does not appear to be a vital factor.

Since no complete fracture of the carpal scaphoid through the waist heals in much less than 8 weeks, plaster immobilization should be continuous for this period. The plaster splint is then bivalved, a roentgenogram is

taken, and the splint immediately reapplied. If the fracture is united, the splint is discarded. If union of the fracture is doubtful, a new circular plaster splint is promptly applied. If this roentgenogram reveals the proximal fragment with its original density while the distal fragment shows atrophy, there is definite evidence of interference with blood supply to the proximal fragment, and prolonged immobilization of the wrist up to 20 weeks or longer may be indicated.

RESULTS OF TREATMENT

Shands reported that 195 of 198 carpal scaphoid fractures treated by trained orthopedic surgeons in 6 Army Air Force hospitals resulted in union, an incidence of 98.5 per cent. Obletz (2) reported in greater detail a series of 28 carpal scaphoid fractures from an Army Ground Force Hospital. He personally followed these cases until plaster splints could be discarded. Union occurred in every case without aseptic necrosis in a single instance.

These 2 instances are, of course, optimum results obtained by experts. Experience gained by the medical officers of the armed forces offers to civilian surgery two salient facts about this fracture: (1) it is a common injury; (2) with complete knowledge of the problem and proper treatment based on that knowledge, a high percentage of those fractures will heal.

Beware of a diagnosis of sprain of the wrist joint! (Fig. 3.)

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MANAGEMENT OF COMPOUND FRACTURES IN THEIR EARLY PHASES

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THE advances during World War II in the management of compound fractures in their early phases came not only in improved techniques of excisional surgery in forward hospitals and in the broad application of specific procedures such as delayed closure of the compounding wounds and surgical incisions or delayed internal fixation of malaligned compound fractures several days later in base hospitals, but of greater importance, in a change of concept for the management of these wounds. Moreover, the basic principles of the science of surgery, itself, were irrevocably reaffirmed.

Battle received compound fractures were all compounded from "without in" and were potentially septic because of the usually present extensive soft part and bone damage, the mud clothing and other foreign material often buried deep in the wound and the prolonged time-lag from wounding to surgery. The wounds and incisions of initial surgery of necessity remained unsutured and reduction of the fractures was usually delayed 5 to 10 days until the wounded men had been transferred to base hospitals. The comparable lesions in civilian life, then, are injuries many hours or days old with unreduced fractures and open and possibly grossly septic wounds.

In the early experience, The Orr-Trueta regimen of closed plaster subsequent to débridement had in general left much to be desired. Slow wound healing by granulation with heavy scar formation was accepted; prolonged wound suppuration with necrosis of living tissue was not infrequent; inadequate reduction of fractures anticipating malunion or nonunion was often accepted; and the prolonged plaster fixation predisposed to extreme muscle atrophy and fixation of joints. Fear of "stirring up" and establishing limb or life endangering sepsis including gas gangrene had prevented efforts at delayed wound closure, at delayed open reduction and internal fixation of unreduced fractures, and even at radical secondary débridement to combat sepsis, the therapy of which had included only prolonged drainage through the open wound, local and systemic sufonamide in an effort to control the bacterial flora of the wound and immobilization.

Based upon previous experiences and observations, during the Cassino and Anzio impasse in early 1944 and the later offensive attendant to the Fall of Rome, the closed plaster—open wound—fear of surgery in a septic field concept was discarded in favor of that of repara-

From Department of Surgery, Washington University.
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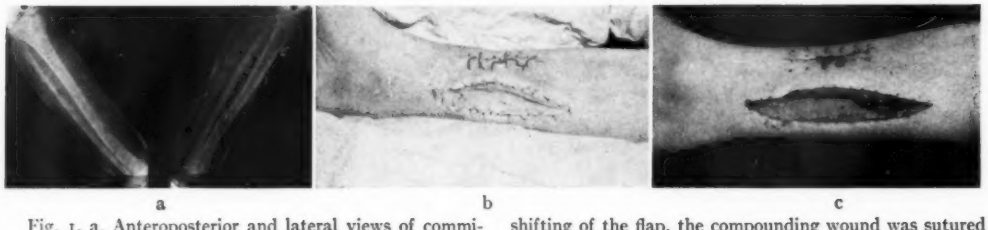

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Fig. 1. a, Anteroposterior and lateral views of comminuted fracture of the tibia at the junction of the middle and lower third, which had been produced by high explosive shell fragments with a resulting gaping wound about 3 inches long. b, Eleven days after wounding and débridement, by means of relaxing incision about 6 inches long and shifting of the flap, the compounding wound was sutured without tension. The defect created by the relaxing incision was at once covered by a split graft. c, Twelve days later, the compounding wound and the grafted defect were healed. Patient returned to duty status about 10 weeks after he had been wounded. (Courtesy J. B. Lippincott Co.)

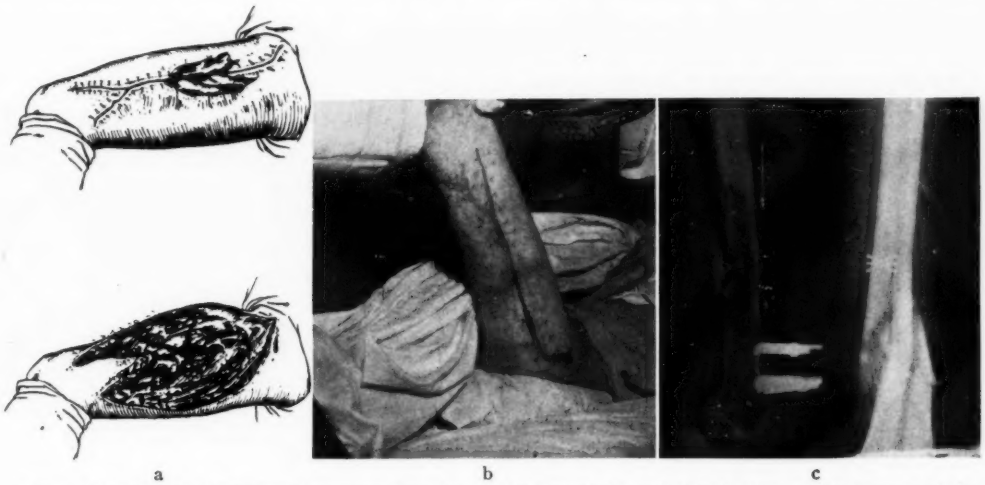

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Fig. 2. a, Drawing of a huge wound compounding a fracture of the femur as it was observed ten days after wounding and initial surgery, and another drawing showing the sutured wound, with dry fine mesh gauze as a drain to residual dead space. b, Seventeen days later, wound healing was complete and a dressing was no longer necessary. c, Anteroposterior and lateral views of the fracture of the femur held in adequate although not anatomical reduction in double skeletal traction. Traction is being made on a wire through the tibial tubercle while vertical lift is being made on the distal femoral fragment by means of a second wire through this fragment.

tive surgery of compound fractures. The new regimen included aggressive secondary surgery in the several days old and possibly septic wound, with delayed excision of dead tissue if necessary, internal fixation of fractures on precise indications and partial or complete closure of clinically clean compounding wounds with obliteration or dependent drainage of residual dead space. Penicillin therapy, systemically, was employed as a safe guard against invasive infection of living tissue by the bacterial flora of the open wound. It was used as a means to a better surgical result and not in an attempt to sterilize an open wound. Whole blood replacement therapy was used extensively to permit prolonged anesthesia and surgery, as an aid in the prevention of chronic sepsis and, presumably, as an aid to wound healing.

The concept for the newer regimen may be stated as follows:

"Wound sepsis results from the septic decomposition of dead tissue including blood clot in dead space. If a wound is free of dead tissue and if dead space is obliterated or dependently drained and if living tissue is protected from invasive infection by an effective antibacterial agent, the bacterial flora of an open wound may be disregarded and any reparative procedure may be performed within the range of recognized surgical limitations without fear of sepsis and with the anticipation of good wound healing."

The experiences and successes achieved in the application of this concept in the management of unreduced compound fractures with open wounds several days after the initial surgery, permit the following conclusions. The supporting data, mostly have been published.

1. In the prevention or eradication of wound sepsis, regardless of the time lag since injury or duration of sepsis, the surgical excision of dead and devitalized tissue and the obliteration or dependent drainage of dead space are prime considerations. Devitalized tissue is the forerunner of sepsis and when sepsis intervenes, reparative measures are doomed to failure, delayed or nonunion of the fracture may follow, and wound healing will be postponed or prevented. Hence, the importance of thorough initial surgery in preparation for reparative surgery several days later.

2. Delayed closure of clinically clean wounds, that is, wounds free of dead tissue and débris

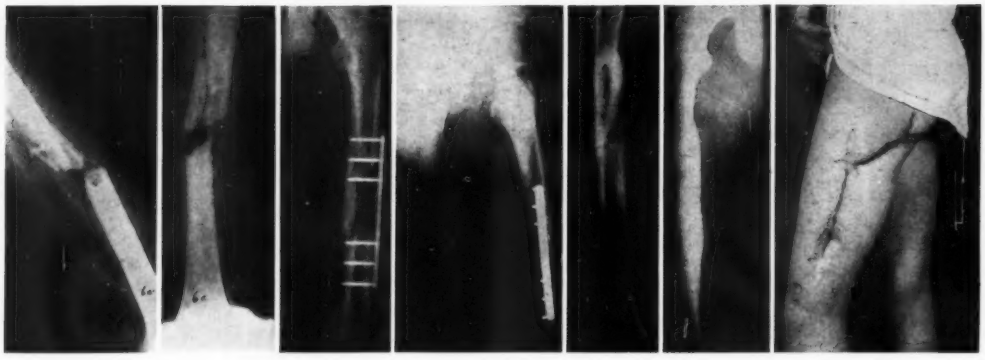

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Fig. 3. a, Anteroposterior and lateral views of a comminuted fracture of the femur which is the site of a gas abscess. The patient had been wounded by a high explosive shell fragment 19 days previously and had received inadequate excisional surgery. Local and systemic sepsis had followed. Although the gas abscess is visible on the roentgenogram, there were no clinical signs of gas gangrene. b, The gas abscess was drained and devitalized tissue was excised through a long posterolateral incision. The dead space about the fracture site was obliterated by fixing the fragments in apposition by means of a six hole bone plate. This illustration shows the fracture partially united 3 months after drainage of the abscess and concurrent plating of the fracture. The wound had been healed since about 3 weeks after the internal fixation of the fracture. c, The wound remained healed and the fracture firmly united in anatomical alignment. Because of some absorption about a screw, as visualized on roentgenograms, the plate and screws were prophylactically removed with immediate closure of the wound and primary healing. d, This illustration reveals the completely healed wound of the thigh with some excessive scar formation which required later excision and subsequent repair. This end-result is a triumph for the principles of reparative surgery.

and of signs of invasive infection, is surgically sound provided dead space is obliterated or dependently drained and excessive tension is avoided. The sliding or advancement of flaps to permit closure without tension is often worthwhile. Therefore, given a clinically clean compounding wound several days after excisional surgery, wound healing by granulation should be scorned, and, if surgical limitations do not preclude, wound closure by suture or skin graft should be performed. Wound healing, while affected by several factors, is a natural cellular growth, provided the wound does not contain dead tissue, dead space, strangulating ligatures, etc. Wound closure may be practiced to the extent to which these qualifying factors can be surgically obviated.

3. The best evidence of adequate excisional surgery is a clinically clean wound 5 days later, the optimum time for delayed wound closure. Within this period, excellent drainage of wound exudate and residual débris is provided, and closure of wounds before the formation of heavy granulation tissue and reduction of fractures before the fixation of fragment ends are permitted.

4. Despite an unhealed wound, inadequate reduction of fractures need not be accepted if it is preventable by open reduction with or without internal fixation. Reduction of the fracture eliminates the dead space about malaligned fragment ends, avoids subsequent manipulations which may produce additional devitalized tissue and anticipates minimum deformity. Internal fixation is detrimental to wound healing, only as devitalized tissue is created in its application or as it interferes with soft part coverage of denuded bone.

5. The regimen as a whole may be expected to achieve minimun sepsis, rapid healing of wounds with minimum scar, maximum reduction of fractures, and maximum functional restoration of the extremity. In this experience, no loss of limb or life attributable to the aggressive surgery was reported.

In summary, reparative surgery of compound fractures represented a major advance in World War II. Under its principles, the spotlight was moved from the bacterial flora to the pathology of the open wound and a surgical approach was established for the management of septic compound fractures. By

judicious application of these principles, that is, the excision of dead tissue, when and wherever it is found, obliteration or dependent drainage of dead space, staged closure of wounds, atraumatic technique with fine hemostats and fine ligatures, pressure dressings, adequate reduction and immobilization of fractures, and precise splinting and with the adjuvant use of penicillin and whole blood, the objectives of the regimen were achieved. Surely, the same regimen under the same principles is applicable to many compound fractures of civilian life which are seen many hours, days, or weeks after injury has occurred and particularly to those with established sepsis.

OSTEOMYELITIS FOLLOWING COMPOUND FRACTURES

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THE changes which have been brought about in civilian practice with respect to osteomyelitis complicating compound fractures have resulted from the application of sound surgical principles and careful attention to detail. Many believe that the advances made in the treatment of these cases are the result of sulfonamides and penicillin. This is not wholly true, for while the antibiotics have played an important part, good surgical care has been of paramount importance. Antibiotics are best applied systemically and there can be no doubt that a patient in poor general condition does not respond as well to these agents in combating infection as one in a good state of health. In patients who have had acute blood loss or with hemoglobin values low because of long continued infection, it is necessary to give adequate blood transfusions if antibiotics are to be of value.

A debilitated patient is a good host for bacteria. A healthy one resists invasion by organisms. Compound fractures are severe open wounds. The fundamental principles underlying open wounds apply whether the bone is involved or not. The realization and adoption of these principles have resulted from experiences in World War II. Wounds seen early, carefully cleansed of as many contaminating organisms and foreign bodies as is possible and the devitalized tissue carefully débrided, are best closed primarily. If this seems not feasible, secondary closure (1) of the wound after several days is advisable. If large defects in the skin or soft tissue result, immediate skin grafts assist the wound to heal kindly even though they may need replacing later with a full thickness sliding or pedicle graft. Obviously, good principles of fracture and wound care must include immobilization. This can, and should when possible, be accomplished without the use of screws or plates. Large dead spaces must be obliterated (3) and when this is not possible, dependent drainage must be afforded to minimize the complication of osteomyelitis.

Chronic osteomyelitis resulting from compound fracture actually is less frequent today than it was before the war, because these principles mentioned above have been more widely recognized as a result of the experiences of World War II. The best treatment for this condition is prevention and careful attention to principles of care of wounds. This is the best prophylaxis we have.

Chronic osteomyelitis should not be confused with hematogenous osteomyelitis which presents an entirely different problem. The two conditions are separate entities and have different clinical, pathological, radiological and surgical considerations. Unlike hematogenous osteomyelitis, this type practically never metastasizes but remains an infection within the bone locally. The treatment of es-

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tablished osteomyelitis following a compound fracture is a problem in the care of the local area supported by systemic treatment to aid in combating the infection and supporting the patient constitutionally. Open drainage with removal of infected areas by saucerization permits drainage after the infection has become localized. This is a principle similar to the treatment of localized infection of other parts. A lesson which has been learned from World War II is that large open defects must not be allowed to remain to depress the vitality of the patient. Skin grafts should be applied as soon as clean granulations have covered the drained area to minimize loss of fluid and discomfort to the patient. These should be applied early even though they are not sufficient in themselves to give good permanent coverage to the area. When such wounds have been properly covered, the patient is more comfortable and early reconstructive surgery can be accomplished with the aid of antibiotics.

Prior to World War II it was considered poor surgical judgment to attempt reconstructive surgery in the area where infection had taken place because of the possibility of reactivating the infection. On one of the large orthopedic services (2) of a general hospital in the Zone of the Interior, 90 per cent of the procedures were done through the original incisions with approximately 5 per cent flare up of infections. Bone grafting to fill defects was also performed 6 to 8 weeks after wound healing. This has been made possible by general supportive measures and the use of sulfonamides and penicillin systemically. The value of appropriate chemotherapy before and after operation in the care of osteomyelitis cannot be stressed too strongly and prolonged administration is of definite value (5).

Reconstructive surgery of the skeletal system should not be done in the presence of draining sinuses, open draining wounds, or any clinical evidence of wound infection. This concept is no different than it was before the war. Penicillin or sulfonamides cannot be expected to be of value in the presence of undrained abscesses, the presence of sequestra, detached fragments of bone with aseptic necrosis or any other foreign body.

Frequently large open wounds with considerable loss of skin, muscles, tendons, nerves, or blood vessels, with bone trauma may be diagnosed as osteomyelitis incorrectly because of the constant drainage or "weeping" from granulation tissue (4). In such cases the drainage will usually stop when the wound is closed by a skin graft if osteomyelitis is not present.

The differences in the care of compound fractures in World War II as compared with World War I are striking. In compound gunshot wounds during the first year of World War I, the total mortality was reported to be about 60 per cent (6). With emergency splinting on the battlefield, the mortality was reported to be about 12 per cent at the end of the third year. During and following World War I, compound fracture wounds were débrided and packed open with vaseline gauze with immobilization by plaster. This continued as the accepted form of treatment even during the late Spanish Civil War (7).

The present concept in the treatment of compound fractures, which has resulted from World War II, has decreased the morbidity and the incidence of chronic osteomyelitis. The application of the principles usually accepted for other infected wounds, as well as the use of chemotherapy, has improved the results in cases of chronic osteomyelitis.

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APPLIED ANATOMY IN EYE SURGERY

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APPLIED anatomy serves a twofold purpose. It gives a precise basis to those occurrences and procedures that especially involve anatomical knowledge; and, in addition, it converts an otherwise unusually dull subject into one of interest by associating it with something manifestly useful and practical.

The student of anatomy has a somewhat hazy, fanciful notion that his study of anatomical structure will, in some way and at some future time prove useful to him. By incorporating with it its surgical application he is made aware of its value in very much the same way as a series of experiments in laboratory physics relates to sheer theoretical, scientific data.

While it is assumed that eye surgeons, in general, are acquainted with most of the premises which I am presenting, it is with the hope that the memory of the dissecting days which have been growing a bit gray with some of us will wish to recall some of the anatomical matters which have the most direct bearing on surgical practice.

In surgery of the lids we must constantly bear in mind the delicate nature of the skin as well as the changes which come with advancing years which have a direct connection with surgical performance. The skin of the eyelid is the most delicate in the body, pale and loosely attached. The foreskin approaches it most nearly in texture. However, it is not wise to use foreskin for lid replacement because, for some unknown reason, it nearly always becomes deeply pigmented. If not much is needed, the skin of the opposite lid is ideal if available. Probably next in order is that just back of the ear, or that from the inside of the arm.

In old age the skin atrophies and loses its elasticity due to atrophy of the elastic fibers. This sometimes induces spastic entropion, since the overaction of the orbicularis has no resilient skin to overcome it. The Ziegler cautery is effective by causing the skin corresponding to the lower margin of the tarsus to adhere to this border so that it will not curl up and roll over the lid margin. In like manner, cauterization of the conjunctival side in hypertrophic ectropion probably causes the conjunctiva to attach itself to the inner border of the tarsal plate. Sometimes in advanced age there will be considerable tearing with a patent drainage canal, often due to lax skin plus a hypertrophy of the conjunctiva. Making only a few punctures immediately inside the canaliculus will bring in the lid margin just enough so that the lower punctum will contact the globe and again siphon off the tears.

It is well to contemplate the width of the tarsal plate in selecting the type of operation for correction of contractile entropion. The tarsus of the lower lid is much narrower than that of the upper; the width of the normal upper being about 10 millimeters and that of the lower about 5 millimeters. Hence, in surgical correction of the upper lid, where the tarsus is still wide, we may attach the cut edge of the skin near the lid-margin to the top of the cleaned tarsus and have a right to expect a satisfactory result. This may be further improved by removing the thickened orbicularis attached to the tarsal plate, producing a wider palpebral fissure. The lower tarsal plate is seldom wide enough to justify utilizing this method, so the modified Green-Ewing method is recommended, as this does not require a wide tarsus.

The eyebrow is thick and curved so as to protect the eye from sweat and blows. It also helps shade the eye from excessive light by bending over. It should not be plucked; and if destroyed by injury should be restored for this and cosmetic reasons. The lashes serve the same purpose and need not be trimmed before surgery. It is often a great advantage to grasp the lashes after operation to pull the lid away from the eye in closing it. The lashes can be replaced by a narrow graft from the

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brow, or from the hair line back of the ear. Recently, Goldzieher reported some preliminary experiments he made on the skin of three elderly women, after some previous experiments on dogs. He applied two estrogenic substances, estradiol and stilbestrol daily to the inner areas of the arms and thighs for a period of 6 weeks. Small sections of the skin taken from these areas showed restoration of the width of the epidermis, the number of cell layers increased, the individual cells larger and the elastic fibers more numerous.

I have seen the skin of the upper lid so lax that it drooped down and cut off some of the temporal field. For this reason, as well as for appearance sake, a strip of it was removed.

The levator palpebrae is inserted in the skin of the upper lid, the lower third of the tarsus and along with Mueller's muscle, to the upper edge of the tarsus. It is mainly these latter fibers with the attached aponeurosis that we use in Cannas' operation, where the paralyzed levator is attached to the tendon of the superior rectus.

The lymph channels from the upper lid pass through the preauricular node; those of the lower lid, the submaxillary node (Treves). This is important in differentiating the lead of drainage in infections and sometimes helps in locating orbital infections where the septum orbitale has been penetrated.

Paralysis of the sixth nerve is particularly associated with fractures of the base of the skull, owing to its long course beneath the dura and its close confinement beneath the petrosphenoidal ligament. In fact, it was Pannas who first recognized that a fracture of the base of the skull might be manifested by a paralysis of the sixth nerve alone. Crepitus of the lids usually denotes fracture of the nasal bone, although fracture of any of the bones forming the nasal sinus cavities connected with the orbit may give rise to air in the orbit or lids.

The orbital cavity is about half an inch wider in the horizontal than in the vertical direction. Therefore it will be seen that there would be more space between the eye and the orbital wall on the sides than above or below; and the greatest interval between the globe and the orbital wall is on the temporal side. For this reason, growths which start on or at the apex of the orbit, or even on the opposite side, may soon find their way to the temporal side of the orbit. Dermoid cysts of the orbit are almost invariably found on the outer side, and although they may appear small, on operation will be found to extend to and be attached very close to the apex of the orbit. It is possible that the orbital septum keeps them within bounds and from protruding forward to any extent.

An intraorbital growth which is not within the intramuscular cone and presents on the temporal side can be reached better through a conjunctival incision than by one through the skin. Sometimes, even with the assistance of x-rays, it is not possible to tell whether the growth is beneath or above the periorbita; and exploration only will determine that fact. If the bone of the periorbita is involved then access through a skin incision is best. To reach growths in the intramuscular cone a Kroenlein approach seems best. In performing this operation, guard against severing the external rectus too far back, or a paralysis may result. If the tendon is cut instead of the muscle belly, it can be sewed together without fear of this happening. In performing evisceration of the orbital contents, it is done easily and quickly by separating the periorbita from its attachment to the wall of the orbit and then continuing to loosen it with a periosteal elevator back to the apex; then cutting off the entire mass from its apical attachment. A clean orbital wall is thus secured and with a minimal amount of bleeding. The cavity must be kept packed sufficiently tight to keep the lids on a stretch, which will otherwise shrivel and atrophy. Of course, if one does not expect to preserve the lids and eventually fill up the orbital cavity, then the lid margins may be freshened, sewed together, and utilized to serve as a covering for the denuded orbital wall.

The conjunctiva is very loosely attached to the globe in man. The reverse of this is noted in operating on animals' eyes; even in monkeys. Man, having a smaller cornea in proportion to the size of the globe than any other animal, necessarily has more of his sclera, covered with conjunctiva, exposed than any other creature. The negro, having a larger eye than

the caucasian, makes this still more noticeable. This makes it easier to perform surgery on man than on animals, as anyone who has experimented on animals' eyes will have observed. There are other reasons, also. This looseness of the conjunctiva is of value in eye surgery in several ways, such as making conjunctival flaps to cover the cornea, correcting mild cases of symblepharon and in other plastic procedures. The distance of the conjunctival fornix from the upper lid margin is from 20 millimeters to 25 millimeters. The tarsal plate is from 10 millimeters to 12 millimeters wide. The distance of the fornix to the corneal margin is 8 millimeters to 10 millimeters. Hence, we have a loose surface of conjunctiva 18 millimeters to 22 millimeters wide from which we may easily take half or three quarters for use of a conjunctival transplant on the other eye socket, or for use in restoring the lining of the canaliculus in a plastic operation for restoring its lumen.

Pterygium is described as a conjunctival growth extending over the cornea. At any rate, the underlying cornea is always involved, with destruction of Bowman's membrane, not only immediately beneath the pterygium, but, according to Fuchs, to a point about 3 millimeters beyond the apparent apex. In my experience, recurrences can be almost invariably prevented if one includes this involved corneal area in his dissection and resects a few layers of the cornea proper beneath the destroyed Bowman's in dissecting off the pterygium.

The most common tumor of the conjunctiva is the naevus. Many are not pigmented and few of them are malignant. About 10 per cent of the tumors are dermoids; and in their removal one must bear in mind that the underlying sclera may be very thin.

While ballooning out the retrotarsal fold with 2 per cent procaine, to which a drop or two of epinephrine has been added, will completely anesthetize both surfaces of the lids for practically all operations on the lids proper, so that no pain will be experienced; when the tear drainage apparatus is involved, more than that is required. For the lids, all of the terminal nerve endings are thus caught supplying the entire thickness of the lids. In order to anesthetize the canaliculus and sac so that no pain will be felt by the patient, to catch all of the nerves supplying the canaliculus one must first instill a drop of pontocaine, then insert a small wad of cotton soaked with pontocaine and epinephrine in the inner canthus and, after waiting about a minute, insert a fine hypodermic needle into the conjunctiva just behind the punctum and slightly temporally to it, inject a drop or two of the solution of 2 per cent procaine; the needle is then advanced in the loose tissue along the course of the canaliculus and drop by drop injected additionally as it is pushed toward the sac. When it reaches the periosteum covering the sac wall a sharp, momentary pain is felt until a drop is injected here. Here, the periosteum is very sensitive as the main branches of the supratrochlear and infratrochlear nerves are encountered. One may now pass the dilator and probe into the canaliculus and down through the sac without the patient experiencing any pain. This, together with the anesthetization of the nasal mucosa by the otolaryngologist is sufficient for the intranasal dacryocystorhinostomy.

In doing an extranasal operation or in removal of the sac, one must block the supratrochlear and infratrochlear and the infraorbital. In passing a probe down the nasal duct one is much more apt to make a false passage with a small probe than with a large one. The lumen of the sac is not just a smooth tube, but is often sacculated in such a manner that the small probe will pass into one of these pockets and penetrate the lining; whereas a larger one might spread the lumen so as to obliterate the defect temporarily and go right on through. Pictures of these anatomical variations illustrated in both Whitnall and Schaeffer should impress this fact on our minds with impelling force.

One of the most frequent sources of failure in performing any type of intranasal tear-sac operation is the failure of the surgeon to make his opening through the bone and sac inside the nose low enough so that the fluid will drain into the nose and not leave a pocket below the opening, holding pus. Another, of course, is failure to keep the opening patent. It is essential that the puncta be in contact with the globe and that the canalicula not be slit, in

order to have complete drainage. The canaliculi are also shortened by blinking, making them wider, and thus helping to carry off the tears. In old age, when laxity of the skin sometimes causes the puncta to drop away from the globe, relief can be had by a limited Ziegler cauterization.

In operations on the cornea it is well to recall that normally, it is thinnest at the center, where it averages about 0.8 millimeter, widening at the periphery to about 1.2 millimeters. It gets thinner with advancing years and may be less than 0.5 millimeter at the center in the aged. This, plus the loss of resiliency, accounts for the sinking in or collapse of the cornea in very old people after cataract incision. A bubble of air injected into the chamber will maintain the normal curvature of the cornea until it has healed.

While Bowman's membrane, if destroyed, never regenerates, it is not an essential part of the cornea for either visual or protective purposes. One may resect a corneal scar and obtain clear vision in its absence with apparently no more hazard to infection in its absence than if it were present. In resecting the cornea for corneal scar, or peeling it off, it is well to bear in mind several things. First, the formation of connective tissue producing the scar creates a much thicker protective shell than the normal cornea. This means that the cut, in preparation for peeling, must be deeper than one would make in a normal cornea, in order to get below the scar formation. Most eye surgeons fail in their corneal resections by not keeping this fact in mind. It also requires more pressure with the knife. It is also less flexible than the normal cornea and cannot be pulled back too much without endangering perforation of the thin, underlying, transparent cornea. Second, in making the crucial incision with the scalpel, don't forget that you are not cutting on a flat surface, but over a convexity with a radius of about 8.0 millimeters. Hence, the handle of the knife must be raised in starting the incision at the limbus and gradually lowered as the cut proceeds toward the opposite margin so as to keep the cutting edge, and not the point of the knife, in contact with and conforming with the corneal curve. This enables one to make his primary cut much deeper without the danger of perforation. Third, and no less important an anatomical point to bear in mind is that the lamellae, normally about 60 in number and from 1.3 microns to 2.5 microns thick, run the entire width of the cornea, crisscrossing with each other at right angles and with very little interlacing; so that they run almost parallel to the curved surface. When one picks up a single section to be peeled off it is essential that he stay in the same layer as that in which he started; otherwise, whenever he cuts across the intervening layers, connective tissue will form with resulting scar. By following proper technique, closely watching the line of cleavage, this is not difficult to do.

In an article by Edward Jackson on "The Function and Structure of the Eye," he stressed the fact that transparency depends on permeability to some substances of the transparent membranes, which included Bowman's and Decemet's in the cornea, capsule of the lens, Bruch's membrane of the choroid, and their impermeability to others. Rupture brings about loss of transparency. The cornea may lose its transparency from transudate or edema, as in glaucoma; exudate, as in keratitis; blood staining from blood in anterior chamber becoming hemolyzed; scar tissue formation and dissolving of the cement substances between the lamellae in the stroma so that the refraction index is interfered with. This latter is probably due to infiltration of aqueous, such as that due to rupture of Decemet's from birth injury. Edema due to entrance of fluid through the epithelium can be differentiated and temporarily cleared by the glycerine test suggested by Cogan. Jackson lays continuous stress on the resilience of the cornea and refers to Salzman's description of the arrangement of the layers, because it is more important and easier to understand when considered as a provision for resilience. Hence, no compression bandage after a corneal cut or cataract operation and keeping the wound elevated. He quotes Ellett, speaking of sutures in cataract operation: "I think it does give a relative assurance against prolapse, but then there is still enough trouble from this source to lead me, after a rather extensive trial of the simple operation, to give up

in favor of the combined operation; except in such cases where the cosmetic effect was a thing to be considered." Jackson used no corneal stitch, relying upon the resiliency of the cornea.

The elasticity of the cornea is greater in the vertical than in the horizontal direction, which may account for the astigmatism in glaucoma, according to Schrender, who found it to be anisotropic; that is, exhibits different properties when tested in different directions.

The cornea is about 12 millimeters in diameter, but the sclera extends 1 millimeter over the edge in the horizontal and 2 millimeters in the vertical meridian. In some cases it extends 3 millimeters or even 4 millimeters over the edge in the vertical meridian, especially so in glaucoma cases. This is a fortunate arrangement in shelving the cornea. This broad limbus is marked in hydophthalmus too.

The epithelium around the limbus is potentially a pigment bearing tissue; this can especially be noted in animals; one may therefore get a pigmented papilloma at the limbus without its being a melanoma.

The sclerocorneal junction is the weakest part of the eyeball. Rupture of the globe at this point may find the lens under the conjunctiva. If the lamina papyracea, which forms the inner wall of the orbit, should rupture, then the eyeball will not rupture. One or the other may rupture, but never both. Decemet's membrane may rupture in birth injuries or in keratoconus and lead to permanent clouding of the cornea, probably through absorption of the interlining cement substance of the layers. Decemet's membrane is easily detached, as happens in doing a trephine or cyclodialysis. It curls under certain conditions and is very elastic. Unlike Bowman's it rapidly regenerates. It is really a crust formation laid down by the endothelium lining the inside of the cornea. This is contrary to the opinion of Eliott, who stated that it and the endothelial lining never regenerated and recommended denuding the endothelium just beyond the limits of the trephine opening so that the opening would not fill up.

At the periphery of Decemet's membrane, in most people, lies the anterior marginal ring as a circular band. It may go only part way around and be rudimentary and can be seen with the gonioscope. Decemet's membrane is more resistant, both to the trephine and to infection than is the stroma. One may find 'warts' (cornea guttata) around the periphery of Decemet's, which can be seen with the slit-lamp and sometimes with the gonioscope. So long as they remain in the periphery they are of no special significance; but if located in the center of the cornea the vision may be reduced as much as down to 20/40 or 20/70; and this must be kept in mind in cases of otherwise unexplainable reduced vision. They sometimes permit the aqueous to leak into the cornea.

There are a number of things which make knowledge of the scleral structure a matter for serious consideration in eye surgery. The sclera is about 0.6 millimeter thick at the limbus. Just back of the insertion of the muscles it is thinnest:—0.3 millimeter or less. This is where the stitches for recession are placed; and fortunately, need not, and should not be deep. Going back to the equator, it thickens to 0.6 millimeter and increases to 1.0 millimeter in the back. At the point of entrance of the optic nerve it is very thin, owing to the perforations of the lamina cribrosa. On account of this inequality of the thickness, one can easily see the futility of using pins in operating for retinal detachment; for, if the pins are set for the proper depth in the thin area, they will not be deep enough where the sclera is thickest. The reverse is also true. The zone overlying the ciliary body is a circular area concentric to the limbus, 5 to 6 millimeters back. The equator is 13 to 14 millimeters back of the limbus. The area of the venae vorticosae is represented by a concentric band 3 millimeters wide and 18 to 21 millimeters back of the limbus; or 5 to 8 millimeters back of the equator. The superior temporal vena vorticosa lies 7 millimeters back of the equator; the superior nasal, 7 to 8 millimeters; the inferior temporal 5 millimeters and the inferior nasal 6 millimeters. These exits can be seen; and in operations for detached retina and posterior sclerotomy these positions must be kept in mind. In posterior sclerotomy it is best to keep near the equator to avoid these and the long ciliary vessels.

Calcification of the sclera is very common in old age and follows absorption of the elastic

fibers in the sclera. This tends to give one the impression of increased intraocular tension by the finger test which is not borne out with the tonometric measurements. Again, the point of the cataract knife may encounter one of these hard particles and interfere with making a satisfactory section. They are usually found on the nasal side as grayish depressions, about 4 millimeters back, but exceptionally may appear further forward near the margin. If this process is far advanced the eye loses its power to adjust itself to lessened volume, as when the chamber is opened and the lens removed; this can be made up by injecting air into the chamber. This factor may account for choroidal detachment, according to Fuchs.

The emissary perforations in the sclera lie 4 to 6 millimeters back of the limbus and are of great importance. Sometimes the long ciliary nerves loop up and look like small, gray tumors in this region. These have been excised under this delusion, which is followed by anesthesia of the corresponding width of the cornea. They can be easily differentiated after having first anesthetized the eye, by grasping the mass, which induces severe pain. Old glaucoma can often be suspected by the enlargement of the ciliary arteries emerging suddenly from these openings, giving the impression of being more greatly enlarged than they really are. New growths of the ciliary body often emerge from the emissaries and give the impression that they are autonomous, localized ones. Transillumination and other means will determine such.

The sclera is loosely attached to the choroid except where the vessels and nerves penetrate it. In making an incision for cyclodialysis, a sharp corneal hook picks up the sclera, making it very easy to cut through the sclera without touching the choroid, since traction with the hook pulls the sclera away from the choroid. Be sure to make the cut in a place free from vessels; which is not hard.

In performing posterior sclerotomy for glaucoma, it is essential to use a knife just as sharp as one would wish for in making a cataract incision and thrust it quickly through into the vitreous, with the blade parallel to the anteroposterior fibers, so as not to separate the retina from the choroid. As the blade is withdrawn the incision is enlarged toward the posterior pole. There is a definite place for this little used operation; one of which is in cases in which, after a drainage operation, the iris or ciliary body has come forward into the wound following an apparently successful operation, causing the tension to rise again. The release of the pressure behind the lens will often cause the ciliary hernia to recede and remain back. There need be little or no bleeding if the technique is carried out properly. This admonition must also be heeded in making the incision for the removal of foreign bodies by the posterior route. In this case the incision must be fully 50 per cent larger than the largest diameter of the foreign body, for one never knows which end is coming first; and it may even come broadside. A long incision heals just as quickly as a small one and does not invite danger of retinal detachment, in my experience, even though one fails to perform electrocoagulation as a preventative measure.

The capsule of Tenon is both membranous and elastic. It is more or less adherent at the attachment of the muscle tendons and, in some places, to the fat of the orbit. Semeraro found that in tests carried out on the cadaver, Tenon's capsule is nonexistant in some cases. This fact may account for the slipping out of the capsule of the implant in many cases of enucleation where the operation seemed to have been well carried out. We have never encountered this condition in the living eye in the many operations involving the muscles, although it does seem to be much less developed in some cases than in others. There is no actual space between the ocular surface of the capsule and the orbital surface opposing it, but the two are connected by a felting of very fine strands of connective tissue. These are loose enough to permit the eyeball to move freely in a limited way; but in extreme excursions, both globe and capsule move together as a whole in a bed of orbital fat, which is loosely connected to the capsule behind. There is a difference of opinion as to how far forward the capsule extends. Sobotta states that it terminates at the upper retrotarsal fold and at the insertion of the muscles. Most authorities agree that it blends with the conjunctiva as far forward as the corneal margin.

Where the vessel sheaths blend with the capsule, they give offshoots to the orbital walls, known as the check ligaments. We shall speak of these in a moment. The septum orbitale is a thin membrane of connective tissue which extends from the entire orbital margin toward the palpebral opening and tends to hold infections to either the orbit or to the anterior part of the globe. The capsule of Tenon, as well as the periorbita and the sheath of the optic nerve, are continuous with the dura. For this reason it is dangerous to perform enucleation in panophthalmitis with marked cellulitis of the orbit, as it may lead to meningitis and subsequent death of the patient. I saw this happen once while I was a medical student. Evisceration is here indicated. In removing the contents of the globe it is imperative that no remnant of the uveal tract remain. The choroid is firmly attached in two places: posteriorly, where the posterior ciliary vessels and nerves enter; and in front where the anterior vessels and nerves pass through the emissaries. These points must be most carefully inspected on conclusion of the operation. When all of the pigmented material has been removed, the sclera will be seen as a white, smooth surface and there will be no bleeding. If the usual enucleation is done and a glass ball is inserted, it is well to figure out just how large the cavity is so that too large a one will not be introduced and be expelled. If we could count on preserving every bit of capsule as far forward as the attachment of the muscle tendons and not allow any for the depth of the sutures, then we might easily put in a 14 millimeter or even a 15 millimeter implant in the capsule. However, anteriorly, the capsule is so intimately connected with the sclera that it isn't detached for several millimeters back of the insertion. Therefore, if one inserts a small ball, not over 12 millimeters in diameter, there will be less stretching of the capsule in sewing it in and more likelihood of it not being expelled. This rule holds good, also, for implanting after evisceration for the reason that taking off all of the cornea and part of the sclera lessens the diameter of what remains. It would seem that Burch's recommendation of leaving the cornea intact and implanting a larger sphere should give a far better result.

In a clean enucleation it is not necessary to sew the tendons together, for they are closely attached to the capsule and fall naturally together whether the capsule be sewed or not. In enucleating a globe for absolute glaucoma where we have a very deep cup, if the nerve is cut too closely one is apt to lose vitreous, for there is no vitreous hyaloid membrane either over the nerve head or the ora serrata. Women's eyes are larger than men's and the negro eye is larger than that of the white man; hence, a slightly larger implant can be used.

In man, the conjunctiva is very loosely attached to the globe except at the limbus. It stretches readily. The capsule of Tenon is supposed to run forward beyond the attachment of the muscle tendons to blend with the conjunctiva. For all practical purposes one can almost forget it is there, unless it constitutes the deep layer under the loose, conjunctival connective tissue which hugs the sclera. In making a flap for sclerocorneal trephine, one must hug the scleral surface closely with the blunt scissors in order to obtain a thick, protective flap. At the point where the sclera and cornea join, the knife is substituted and the cornea split. One can easily determine when the cornea has been reached by its bluish appearance. The same technique for splitting the cornea in a sclerocorneal trephine is recommended as in the resection for corneal scar. If properly done it requires less than a minute's time.

In exposing the muscle tendons for advancement, recession or enucleation, the capsule of Tenon should be disturbed as little as possible and none of it lost. Make the incision in the conjunctiva large enough for freedom of operation, for a large incision heals just as easily and quickly as a small one. When the area to be explored is sufficiently exposed, remember that immediately under the conjunctiva and over the capsule is some loose, connective tissue which will be grasped by the forceps instead of the capsule if it is not pushed aside. To accomplish this, place the flat fixation forceps so that the blades will be closed and parallel to the length of the tendon; press it down on the globe and at the same time, separating the blades, while still maintaining the pressure. It is necessary that the forceps have

a strong spring in order to do this properly. Then, without releasing the pressure, separate the blades about 2 or 3 millimeters and then make increased pressure against the sclera so as to indent it while closing the blades. The forceps will now have a good hold on Tenon's. Keep the grasp firmly, make a snip with the scissors close to the end of the forceps while pulling it slightly away from the sclera; keep the original grasp on the capsule until the hook has been slid under the tendon. The reason the blades must be kept parallel to the length of the tendon is that when the eye is rotated to expose the area, the capsule, as well as the tendon is put on a stretch; which makes it easy to be grasped thus and very difficult if it is attempted against the stretched tissue.

The average distance for the attachment of the recti muscle tendons back of the limbus is, medial 5.5 millimeters; inferior 6.5 millimeters; lateral 6.9 millimeters; superior 7.7 millimeters. Hence, the forceps must be placed far enough back to catch the free side of the tendon. Of course, these measurements vary considerably and, according to Motais they may be as far back as 7 millimeters for the medial and 11 millimeters for the superior. It is better to allow for the maximum than to get too far forward. It is also well to bear in mind the width of these tendons so that, in first placing our forceps in position we will not include any of the tendon fibers. The average breadth of the tendon varies from 9.2 millimeters for the lateral to 10.75 millimeters for the superior. Thus one sees that in placing the forceps it is well to be about 6 to 7 millimeters beyond the estimated center of the tendon to be exposed. While the medial rectus is thickest and strongest, its tendon is also the shortest, averaging less than 4 millimeters in length; while the lateral, which is the weakest, is nearly 9 millimeters long. It also must be noted that the lines of insertion of the tendons are not straight, but are curved, or even wavy and do not lie parallel to the corneal margin. For example, it is easier to approach the tendon of the superior rectus from the medial side than from the temporal, since it is several millimeters closer to the limbus nasally.

The superior oblique attachment to the globe lies just behind that of the superior rectus. Therefore, all one has to do to expose the superior oblique tendon is to engage the attachment of the superior rectus tendon with the hook, reverse the pull by turning the hook and draw the hook backward, thus engaging the tendon of the superior oblique and pulling it forward into the conjunctival wound.

Since the inferior oblique arises from a small depression on the orbital floor, just within the inferior orbital margin, lateral and close to the nasolachrimal canal, it can be easily exposed by a deep incision into the lower conjunctival sulcus; deep enough to strike the periosteum on the floor of the orbit, introduce the hook into the opening until it strikes the floor and then sweeping it nasally until the resistance of the attachment is felt, whereupon it is drawn into the wound.

Stitches for a recession are placed where the sclera is thinnest. Fortunately, the stitches in this case need not be and should not be as deep as for advancement, for there is less pull on the muscle operated upon after than before the operation for two reasons. First, because the tendon is set farther back, and because the muscle is partly paralyzed from handling. If all of these rules are followed out, bearing in mind the anatomical features mentioned, the tendon of any of the muscles, either straight or oblique, can be caught with the first sweep of the hook. Failure to do so means faulty technique.

The attachments of the capsule of Tenon to the margins of the orbit prevent the muscles from entirely retracting and, even when the globe has been removed, give them bases to act upon, thus preserving some motility in the stump. Rough handling of these attachments so as to mutilate these parts of the capsule can result in an ugly proptosis after a strabismus operation; or sinking of the globe after enucleation. When a part of the capsule known as the suspensory ligament of Lockwood is mangled the eyeball drops; or there may be excessive lateral rotation of the globe or upward movement. Instruments should always be sharp, so that clean cuts can be made with the scissors instead of tears. Clean cuts heal easier and are less prone to infection.

O'Connor suggested a novel method of increasing the effect of the Himmelsheimer oper-

ation by utilizing the nasal third of the rectus muscles, turning them under the rectus tendons before sewing them laterally. The objection to this, however, is that it puts even a greater stretch on these transposed portions. A more secure method is suggested for this valuable conception: utilizing the paralyzed, split rectus to attach to the vertical recti and then severing the nasal third of their attachment to the globe. This involves the same principle as the O'Connor method, is easier to execute, and eliminates the danger of tearing loose of the vertical strips.

In operating on the muscles, in order to obtain complete anesthesia, it is necessary not only to instill an anesthetic in the conjunctival sac and inject the intramuscular cone, but also to use a very fine needle and inject a drop or two into the muscle belly itself. While most of the sensory nerve endings terminate near the tendinous attachment, the tendon tissue is too dense for it to spread and complete absence of pain will be accomplished only by injecting into the muscle itself.

In a recent article on "Guides to Choice of Operation for Squint," Sugar stressed Bielschovshy's guide to choice of operation, based on anatomical and physiological principles. They are important enough to repeat here.

1. When a difference in the two eyes under cover can be determined, the eye showing the smaller deviation is the paralyzed one.

2. When the vertical deviation of the paralyzed eye is greater in adduction, an oblique muscle is involved (because the obliques help in adduction) and for the same reason, when it is greater in abduction, a verticle muscle is involved.

3. The image of the paralyzed eye is always seen in the direction in which the affected muscle should move the eye.

4. When tilting of images is marked and tipping of the head greatly increases diplopia, an oblique muscle is nearly always involved.

5. The principal action of a muscle should always be considered.

Klein, in investigations concerning the lens capsule and its importance in the technique of intracapsular cataract extraction, emphasizes the fact that the zonular lamella is a very thin membrane that covers the peripheral parts of the anterior lens capsule and is easily separated from it. The posterior capsule is thinner than the anterior lens capsule; the central area of each is thinnest, the maximum thickness being between the equator and the center. In old age the zonular fibers become fragile and the capsule thicker (there is an exception, that of the Morgagnian, where both become thin). By a special method, he found that the capsule can resist a pressure of 150 to 200 millimeters of mercury. He recommended traction on the lens capsule and simultaneous pressure at the limbus with a hook to rupture the zonule: then, repetition of the maneuver in a different direction. In intumescent and hypermature lenses, as well as in those cases where there has been a previous uveitis, the zonule is so weakened that it is ruptured with a minimum amount of pressure so that the lens can be extracted by the Smith method without touching the capsule. These are the only cases where the Smith method is recommended.

Since the lens capsule is thickest between the center and the periphery, this is where it should be grasped with the Arruga or similar forceps in breaking the zonule. There is a tendency of many surgeons, in order to make sure of securing a firm hold on the capsule, to take too wide a bite. When this is done it stretches the capsule to such an extent that it is more liable to break before the zonule ruptures. The zonular lamellae may extend back as far as the ora serrata and if pulled upon too much can detach the retina or pull a hole in it. This may occur in doing an intracapsular; or even in doing a needling if not done properly. The lamellae may not attach and there may actually be a thickened capsule around the edge of the lens which may desquamate into the anterior chamber and cause glaucoma.

The anterior hyaloid has tremendous stretching qualities and may come forward after the cataract incision and be mistaken for vitreous. If the speculum be immediately removed and traction made by pulling down on the upper lid, it usually retracts and one may proceed with the operation. Here is another advantage of having lashes with which to grasp the upper lid in order to pull it away from the globe. There may be an anomalous

union of the anterior hyaloid with the lens capsule, which proves a detriment to extraction in the lens capsule; for in this case the hyaloid is torn and vitreous exudes. This anomalous condition cannot be determined beforehand.

In the embryo there is a sinus running around the pupillary area and in adult eyes cysts sometimes form in this sinus area, separating the pigment layer. They may manifest themselves by floating down in the pupillary area as a black mass, when we may assume that it is a cyst. If, however, the black mass is seen at the base of the iris, melanoma must be suspected.

Tags near the base of the iris show a reversion to the pectinate ligament in lower animals. Normally, in the human, there are only a few trabeculae in the angle. These may extend from a peripheral iris knob, which at times, is present in the human. If present in a glaucomatous eye, the synechiae will run from it to the angle.

The vessels of the iris run parallel with the radiations: Hence, cutting the iris in the direction of the fibers in an iridectomy causes less bleeding and, at the same time, enables one to make a deeper iridectomy. For this reason I fail to see how a peripheral iridectomy in acute glaucoma can be as effective as a complete one, as claimed by some.

Sugar stresses the importance of knowing the depth of the anterior chamber in glaucoma and describes a method for measuring it by means of the McNair-Bettman portable slit-lamp. The important thing is the angle. Of special significance is the condition of the angle, which can be determined by gonioscopy. Through this means Barkan has developed the operation of goniotomy for congenital glaucoma, which consists of removing occluded fetal meshwork from the angle; promising much for this hitherto almost intractable disease. Anderson's analysis of 84 specimens, finding the canal open in 75 per cent of the early specimens and no trace of it in children over 2½ years of age, none of which had been operated on, strengthens Barkan's warning for early operation in these cases, since the distention of the eyeball tends to obliterate the canal. Barkan makes the distinction between goniotomy in the infant, which consists of removal of fetal remnants from the angle; versus trabeculotomy in the adult, whose object is to incise the angle wall; that is, the trabeculum itself. In the May issue of the *Archives of Ophthalmology* an article appeared by Hughes and Gartner in which they recommended the removal of the aqueous, substituting air, thereby deepening the anterior chamber so that it is possible to perform goniotomy in cases with a shallow chamber as well as in those cases with a wide angle.

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THE MANAGEMENT OF STRABISMUS IN CHILDREN

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IN discussing the subject of the management of strabismus in children I have tried to select those points on which opinions may differ as well as some aspects of the problem of particular interest to me.

EXAMINATION

In the examination of the young child, it seems unnecessary to stress the importance of an accurate record of the vision. Realizing fully the possible sources of serious error, I believe that, in many cases the symbol E, used with care, can give a reliable measure of vision at an early age. Some arrangement that shows only one symbol at a time and one that can be varied freely to avoid a pattern that can be memorized would seem best. E's mounted on translucent plastic squares, and held in front of a weak light, as recently devised by DeVoe,[1] give a convenient and practical method, although it will tend to give a better score than the conventional Snellen chart. If this method of examination is preceded by a little practice at home, even 3 year olds may give satisfactory responses. It is possible, however, to make useful deductions about the vision without such measurements. If the squint is firmly monocular, it is a safe assumption that the squinting eye is amblyopic to some degree. On the other hand, if there is alternation, even in only one field, one can assume approximately equal vision.

In studying the nature of the squint, the corneal reflexes can be of great value. They are best observed by holding a small flashlight directly in front of the patient, approximately at the end of the observer's nose. In the very young patient, this is, of course, the only method of examination that can be used. But at all ages, it gives a constant objective check on what the eyes are doing at all times and we should cultivate the habit of watching these reflexes.

From the Eye Institute of Presbyterian Hospital, New York.
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[1]Personal communication.

In children of 1 or 2 years of age, in addition to observing the corneal reflexes to determine the type of deviation and the fixation, an attempt should be made to study the excursions. It is frequently impossible to bring out abduction. The monocular case will not bother to abduct the squinting eye, while the alternator looks to the left with his right eye and to the right with his left and has no incentive to use abduction. Yet it is essential to rule out paretic or absent external recti. Usually, total occlusion of the fixing eye or of each eye alternately, for a short period, will demonstrate that full abduction is possible. Probably you have all shared my experience that the more you look at children with squints, the higher percentage you find with overaction of one or both inferior obliques. This is brought out by carrying the eyes well to the side and up, at the same time shielding the eye of the opposite side from fixation. The splendid article by Adler in the last transactions of the American Ophthalmological Society explains the condition.

MEASUREMENT

Measurement of squint is of particular interest since I believe that the most accurate possible measurements are an essential step in our quest for more perfect surgical results, even though at present our surgical methods do not yet justify such accuracy. For our youngest patients, we must rely on the displacement of the corneal reflex, as described originally by Hirschberg. This must of necessity be a crude measurement, but if it is the only one available, we must make it as reliable as possible. Practicing on older children, checking it against the cover test, will improve our judgment in using it. Transposing and rechecking Hirschberg's figures, I consider that each millimeter of displacement on the cornea is equal to 16 prism diopters, using 6 millimeters as the radius of the cornea.

The next test, in terms of the age of the patient, is the prism reflex test. This was first

described by Krimsky. A prism is held in front of the fixing eye, with the apex toward the nose, in a convergent squint. This causes the eye to shift toward the nose to resume fixation and the squinting eye will make a corresponding shift away from the nose. Thus using the fixing eye as a handle, and varying the size of the prism, the squinting eye can be moved back and forth until the corneal reflex is accurately centered. This is exactly what is done with a Priestly Smith tape but the prism reflex test is considerably simpler to use. It can be used only for monocular squints. The perimeter is still the best method for obtaining distance measurements on a patient with poor fixation in one eye.

As soon as the child is old enough to cooperate (3 to 5 years of age) and if both eyes are capable of fixation, the cover test of Duane is the method of choice for measuring squint. This method has been admirably set forth in the writing of the late James W. White. It will do all that he has claimed for it and we should all learn to rely on it very largely in the measurement of squint.

TREATMENT

Regarding the actual treatment of strabismus, it hardly seems necessary to urge that these children be seen as early as possible after 6 months of age. Unfortunately, some pediatricians still advise waiting to see if a deviation will be outgrown but I believe that their number is diminishing. Possibly not much will be done in the way of treatment until the child is a year old, but it is worth while to see him earlier to watch developments. Occasionally operation will be indicated, as will be discussed later. Whatever therapeutic measures may be required, it is undeniable that the earlier they are employed, the more complications, such as amblyopia, abnormal retinal correspondence and muscle changes will be avoided or minimized and the chances will be better for binocular vision and fusion.

I believe that there is general agreement as to the value of giving glasses that fully correct any significant hyperopia or astigmatism. The accommodative squints do not often appear before 2 years, but the glasses should be worn as early as possible.

Amblyopia. In this air-minded age, good visual acuity in both eyes has become even more essential. This means that the correction of amblyopia ex anopsia is the responsibility of the ophthalmologist. Such correction can be accomplished in the majority of patients under 8 if time is taken to impress parents with its importance. Again, the earlier occlusion is begun, the more quickly will the result be obtained. As mentioned above, it is not necessary to wait until the vision can be measured to know that you are dealing with amblyopia. If the squint is solidly monocular, you can assume that the squinting eye is amblyopic and proceed with occlusion. By watching the behavior of the eyes when the occluding bandage is changed, one can proceed with confidence and safety. As long as the originally fixing eye resumes fixation whenever the bandage is removed, the objective has not been achieved. In young children, it is easy to cause fixation to shift to the previously squinting eye, an event that distresses the mother but pleases the doctor because it proves that both eyes are sound. There is no way to differentiate amblyopia ex anopsia from a true amblyopia in little children, so all patients should have a trial course of total occlusion for at least 2 months. At the beginning of occlusion, anything short of total occlusion, 24 hours a day, is apt to be a waste of time. It is easier for the child to have it on all the time; it will bring the result most rapidly. A firm adhesive bandage, over cotton, is the occluder of choice. Later, and this will vary from 2 to 8 weeks or more, various occluders can be used on the glasses, but I rely largely on atropine in the better eye with paper on that spectacle lens. It should be apparent that atropine alone will be successful only in cases of slight amblyopia or extreme hyperopia; when combined with an occluder on the spectacles, the drug will only succeed after the squinting eye has acquired the ability to fix.

ORTHOPTIC EXERCISES

It is extremely difficult if not impossible to get an idea of the true value of orthoptic exercises from the literature. There is no way to reconcile the highly optimistic report of results obtained by Berens and his associates

with the completely negative report of Fowler; both are competent reporters but they cannot possibly both be right. Unfortunately, in the majority of articles reporting indications for orthoptic exercises and the results of orthoptic treatment, definitions and classifications of cases are either absent or so indefinite that few conclusions can be drawn. There is yet no unanimity about the value of orthoptics. In the opinions of many ophthalmologists, it has failed to achieve an established position in the treatment of squint. Yet it is being used by far too many reliable clinicians to be ignored.

It has not been my practice to use orthoptic exercises routinely in healing strabismus. This decision was reached after experience gained while in charge of an orthoptic Clinic at Vanderbilt Clinic, in New York, from 1935 to 1938, while serving on the American Orthoptic Council for several years and from reading the orthoptic literature closely. There are two principal reasons for my decision: First, it was not possible for me to predict the outcome of orthoptic training with sufficient accuracy to feel justified in prescribing it for my patients. No doubt there are orthoptic technicians who can make fair prognostications of their own management of these cases. However, if an ophthalmologist is going to use this method of treatment, he too must be able to tell his patient approximately what he has a right to expect in a given time. At the present time, I am unable to do this.

My second reason is that I do not have the facilities for carrying out the treatment. Most of us do not have a sufficient number of muscle cases to employ a full time technician. The obvious solution is for several ophthalmologists to pool their cases and resources and set up a technician in a separate office. This has been done in a few cities with notable success but, at present, I know of only one technician in New York to whom private patients can be sent. As you may surmise, she is far too busy to do more than see an occasional case for any one doctor.

In spite of other practical obstacles, there is no doubt that there is value in orthoptic exercises; that some patients with accommodative squint would get rid of their glasses more quickly and more certainly with training; that some patients with small deviations could avoid operation; and more patients could achieve binocular single vision with fusion after operation. We need to learn a great deal more so that we will know which cases offer reasonable prospects of success and so that accurate prognoses can be given to our patients. In this direction, I hope to see many new orthoptic clinics established.

Age and indications for operation. In recent years, the trend in this country has been toward earlier operation until it is now not uncommon to do the operation while the child is in the neighborhood of 1 year of age. These early cases are of course those born with the squint, which means a true muscle anomaly. These are nearly all marked deviations with frequently a vertical complication. While refractive errors can hardly play a part at this age, it is probably wise to do retinoscopic and fundus examinations, under ether if necessary. It is usually apparent that nothing but surgery will correct the deviation. The parents are distressed and embarrassed over the appearance of their baby. The avoidance of secondary muscle changes and the chances of re-establishing binocular vision, all greatly outweigh the disadvantage of operating without a complete analysis of the case. This analysis could be gained only after long delay.

In the larger group of cases that come on gradually after the second year and have more or less relation to accommodation, operation should be delayed until other measures have been tried. Glasses should be worn for several months; amblyopia corrected; and possibly there should be orthoptic training. When these measures have been carried out, abandoned or considered unsuitable, operation is indicated, regardless of the age. However, for psychological reasons, great effort should be made to complete the essential preliminaries and to perform the operation before the child enters school. For the same reasons, it may be desirable to shortcut the preliminaries in some cases, and operate earlier. A serious objective to orthoptic training is that valuable time may have to be lost in waiting for the child to attain an age when exercises can be given.

Only in those cases with high hyperopic errors (usually +4 or more) where the deviation

is largely eliminated by glasses, should the operation be postponed indefinitely. The majority of these children will not require operation and at around 15 years, they will be able to remove their glasses when not doing close work. When the occasional operation becomes necessary, only that portion of the deviation remaining, when glasses are worn, should be corrected. Care must be taken not to weaken convergence unduly.

Choice of operation. It is almost impossible to tell someone else what procedure to do for a given deviation. Each surgeon must decide which of the many modern techniques makes the most sense to him and which he can do best. Exactly similar results can probably be obtained in several ways. Mention of a few general principles may be helpful. For the usual concomitant esotropia which measures a little greater for *near* than *distance*, a resection of the externus and a recession of the internus of the same eye are my choice. I operate on the squinting eye because it makes sense to the parents and the muscle changes will be in this eye. If there is a conspicuous overaction of the inferior oblique of that eye, a recession of this muscle at its insertion is done at the same time. Even if the overaction is bilateral, the inferior oblique of the fixing eye need not be touched as its overaction rarely becomes manifest. When the deviation is greater for *distance*, emphasis is placed on the resection of the externus; when much greater for *near*, the recession of the internus is stressed, or possibly divided between the two eyes. In alternating esotropia, it seems logical to operate on both eyes, and while this would probably give the best result, it is not practical to operate on 4 muscles when not absolutely necessary, so I would handle them like the monocular squints. An exception to this is the very young alternator who uses the right eye to look to the left, and the left to look to the right, and never abducts either eye. Here, bilateral recessions of the interni are indicated. In alternators, there will frequently be bilateral overaction of both inferior obliques. If these are approximately of equal amounts and not extreme, they can usually be ignored.

The question of how much to do to correct a given deviation is constantly asked by the Residents. The best suggestion that I can offer is the figure that Dunnington and I reached several years ago when we analyzed a fairly large series of our operations. We found that when we did a 10 millimeter resection of the externus and a 4 millimeter recession of the internus, on the same eye, we averaged 40 diopters of correction. This is only a rough guide but it provides a starting point.

While I do not want to stress technique because I believe that the many minute variations that have been described are unimportant, I do want to make an appeal to each surgeon to perfect his own technique. It is important that he be able to reproduce an operation with precision, as that is the only way that he will be able to find out just what his operation will do. Eventually he will be able to translate accurate measurements into definite, predictable surgical results. I have been using the resection described by Lancaster, for several years. Being able to tie the 2 mattress sutures while the tendon is still held firmly in the muscle clamp appeals to me as safer and more definite than other methods. For the recession of the internal rectus, I use two single-arm sutures: one in the upper third of the tendon, secured by passing the needle through the tendon a second time, and the other in the lower third of the tendon; both placed as close to the insertion as possible. Great care is used at this point to waste as little of the tendon as possible. The sutures are then passed through the superficial fibers of the sclera, a measured distance from the stump and at least 8 millimeters apart so as to spread the tendon flat. The conjunctiva is closed with care, 3 to 5 interrupted sutures being used. The recession of the inferior oblique is done by the method described by White (9). It seems to offer the best possibility for a graded weakening of this muscle. Avertin and ether anesthesia is routine. No. 0000 plain catgut sutures on atraumatic needles are used throughout. I bandage only the eye operated upon and do not use atropine. The bandage is changed on the second operative day and removed entirely on the 4th or 5th. These details are mentioned only because they may be of interest, not because I believe that they are necessarily the best.

SUMMARY

Early examination by means of the symbol E to test vision, and measurement of the deviation by means of the corneal reflexes and the prism reflex test are emphatically recommended.

Treatment should start as early as possible and should include occlusion in all cases of monocular squint.

The reasons for not using orthoptic exercises routinely are stated.

Operation can be done safely at 1 year, and in certain cases gives definite advantages when done early.

The indications for operation have been discussed and my choice of operations has been given briefly.

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A NEW TYPE OF BASKET IMPLANT FOR USE AFTER ENUCLEATION

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CONSIDERABLE thought has been given recently to the possibility of improving the cosmetic result in enucleation or evisceration procedures. It is probable that out of this interest will come improvements that will stand the test of time and use.

The ideal cosmetic result should achieve the following:

1. Wide range of co-ordinate movement with the remaining eye.
2. Instantaneous movement over a short range.
3. Normal lid contour, i.e. (a) no sagging of lower lid, (b) no sinking in of upper lid.
4. Permanence of the implant. This implies that it shall not migrate or be extruded.

No procedure, whether enucleation or evisceration, with or without an implant has achieved all of these results up to this time. Different procedures have been devised as recently revealed by Dimitry that have resulted in a good movement of the stump but the problem has always remained of transmitting this movement to the prosthesis. The basket-type implant to be described is a step toward improving the transmission of this movement from the stump to the prosthesis on what might be called conventional lines, i.e., the prosthesis is completely enclosed in tissue.

The purpose of a basket implant, with a resulting depressed area in the socket, is to give the prosthesis, which has a stud projecting posteriorly (Fig. 1), a grip on the stump. This necessitates, of course, a custom-designed prosthesis and, in addition, imposes new problems of design on the artificial eye maker. This is due to the fact that there is more ability of the cuplike depression to move the artificial eye than there is space in which the eye can move. Thus, it is necessary to adjust carefully the size and shape of the prosthesis in order to use the minimum amount of space and still maintain a normal fissure. This is facilitated if no attempt is made to fill out a depressed upper lid with the prosthesis, but that is left to the surgeon.

The standard basket now used is shown in Figure 2A and B. It is made of lucite (methyl methacrylate) and measures 11 by 15 millimeters. This size seems to be the best whether the eye to be enucleated is large or small. The anterior edge is slightly thickened, the sides of the basket are fenestrated to allow for invasion of tissue. In addition, there are 3 holes in the bottom, measuring 1 millimeter in diameter, 2 of which are for sutures. Larger and smaller baskets have been tried, but a tendency to reduce movement has resulted in either case. Other materials are being tried, but lucite has been found satisfactory up to the present time. A lucite button, measuring 5 by 8 millimeters, with four 0.8 millimeter holes (Fig. 2C) is used to tie the sutures through and maintain the depression during healing. Three double-armed sutures are used: black No. 0 nylon, blue No. 00 dermal and purple coarse dermal. These are used because of their greater strength and smoothness, allowing sutures to be pulled up without breaking. They are of different colors to permit ready identification. One inch (2.5 cm.) straight intestinal needles are used to allow their passage through the plastic button.

At the end of the operation a special plastic retainer (Fig. 2D) is placed inside the lids after the method of Gifford. This greatly reduces postoperative edema, keeps the basket centered, and completely prevents any prolapse of the conjunctiva. The average operating time for this procedure is the same as for any implantation procedure, namely, 22 to 25 minutes.

Two baskets slightly smaller than the standard have been placed inside the sclera after

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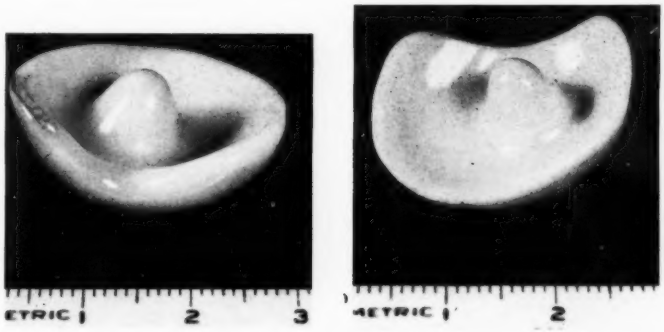

Fig. 1. Plastic prosthesis showing projecting stud on posterior surface.

evisceration. No advantage accrued as far as movement of the stump was concerned, and the depression into which the stud of the prosthesis fits was considerably smaller. In addition, there was extreme postoperative edema, involving the entire side of the face, which lasted 7 to 10 days. I have seen 2 cases in which a ball implant was placed in the sclera with extremely good movement, practically as good as that of the normal eye, but because of the smooth contour only a small amount could be transmitted to the prosthesis.

The muscles are not sutured in this procedure. Figure 3 shows the posterior view of a basket implant removed at autopsy 8½ months after operation from a patient who was killed in an automobile accident. It will be seen that all the muscles, including the obliques, are attached near the rim of the basket.

OPERATIVE PROCEDURE

Anesthesia is induced by intravenous injection of sodium pentothal and retrobulbar injection of 2 cubic centimeters of 2 per cent procaine hydrochloride.

The eye is prepared in the usual manner. A speculum (Weeks) is inserted, the conjunctiva dissected from the limbus, and the dissection carried to the fornices in all directions. The rectus muscles are then isolated and cut free from their insertions. The conjunctival opening usually is enlarged nasally and temporally about 2 millimeters to permit passage of the globe. The globe is grasped with fixation

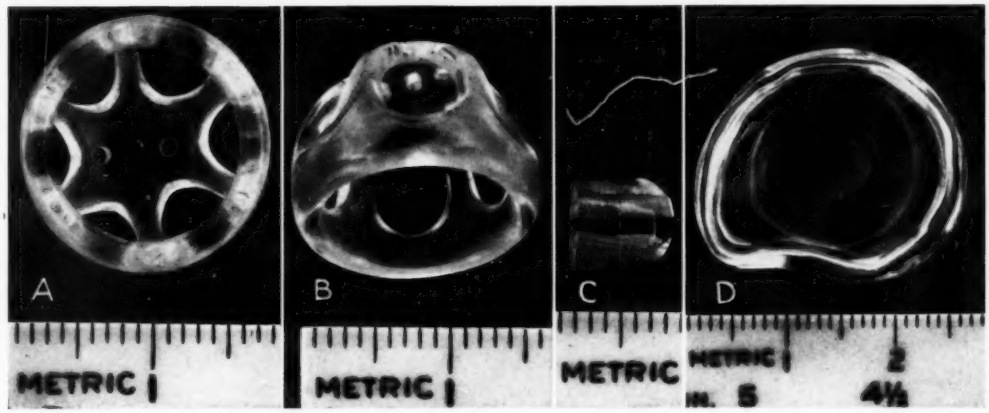

Fig. 2. A, Top view of lucite basket; B, side view; C, lucite stud; D posterior view of lucite with central depression for stud.

Fig. 3. Posterior view of basket, implant removed at autopsy 8 months following implantation showing muscles attached to anterior edge.

forceps at the tendon of the internal rectus muscle and the nerve cut with enucleation scissors. The prolapsed globe is then freed from the oblique muscles and removed.

A dry gauze sponge and a little pressure usually reduce the bleeding quickly to enable one to inspect Tenon's capsule (Fig. 4).

The basket, with one black nylon suture, size No. 0, fitted with two straight 1 inch

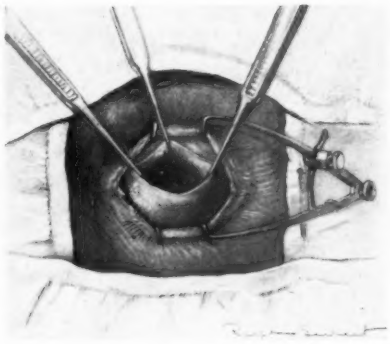

Fig. 4. Tenon's space exposed, ready for insertion of basket implant.

intestinal needles, is then placed in Tenon's capsule (Fig. 5). The upper suture is brought through a firm bite of Tenon's capsule at 12 o'clock and out through the margin of the conjunctiva. The lower suture is brought out similarly at 6 o'clock.

A blue No. 00 dermal, double-armed suture with 1 inch intestinal needles is then carried through Tenon's capsule and the conjunctiva about 2 millimeters on either side of the black suture which was placed at 6 o'clock (Fig. 6A). Each suture is then carried through in a simi-

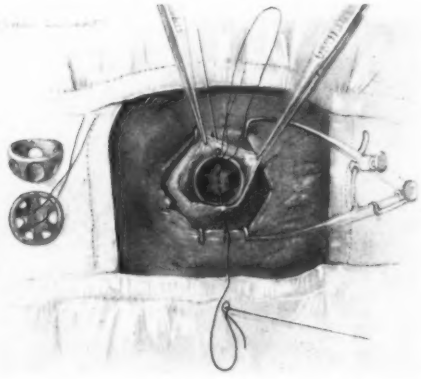

Fig. 5. Basket with No. 0 black nylon suture inserted. Suture carried through Tenon's capsule and conjunctiva at 12 and 6 o'clock.

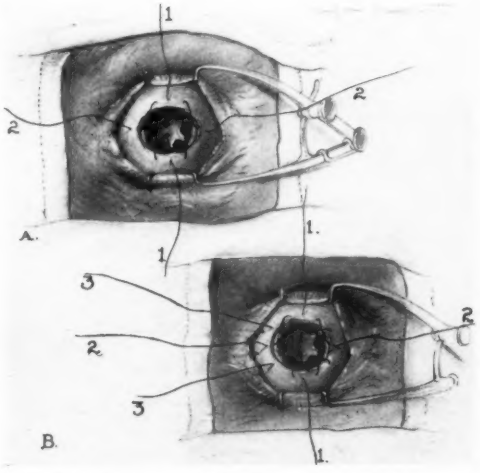

Fig. 6. A, Blue dermal mattress suture, 2, carried through Tenon's capsule and conjunctiva on either side of black nylon from within outward and finally through Tenon's capsule and conjunctiva at 3 and 6 o'clock.

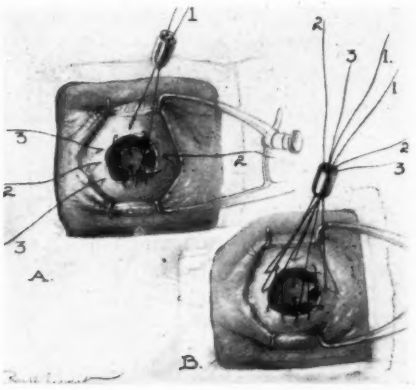

Fig. 7. Black nylon suture, *1*, carried through holes in lucite stud; B, purple dermalon suture, *3*, carried through the same holes in stud as suture, *1*; Blue dermal suture, *2*, carried through the other two holes in lucite button.

lar manner at 12 o'clock. The suture on the right side is now carried through Tenon's capsule and the conjunctiva at 3 o'clock on the same side and the suture on the left at 9 o'clock.

A purple dermal (coarse), double-armed suture, similar to the blue dermal suture, is now placed about 2 millimeters on either side

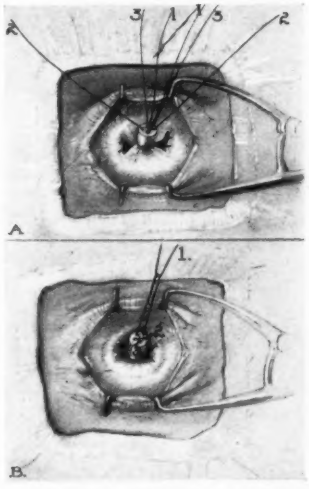

Fig. 9. A, Suture, *2*, pulled up, imbricating Tenon's capsule and conjunctiva vertically. B, Suture, *2*, tied and cut. Suture *3* pulled up tight and cut through, imbricating Tenon's capsule and conjunctiva horizontally and closing the basket opening.

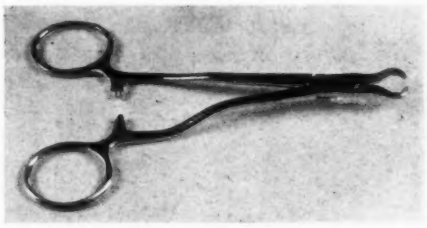

Fig. 8. Button holder.

of the blue suture at 3 o'clock, the needle taking similar bites of Tenon's capsule and coming out through the conjunctiva. These two sutures are now carried across above all other sutures and brought out 2 millimeters on either side of the blue suture at 9 o'clock (Fig. 6B).

These two mattress sutures (blue and purple) are placed as outlined in the preceding paragraphs, so that when they are pulled up they cause a double imbrication, or folding, of Tenon's capsule and the conjunctiva and the black sutures still come out through the upper layer after this has been done. All sutures are carried through the lucite stud, as shown in Figure 7A and B. Sutures *1* and *3* pass through the same two holes and suture *2* through the other two holes.

While the assistant holds the button with the lower end at the level of the rim of the basket with the button holder (Fig. 8), the blue suture is pulled up, tied, and cut (Fig. 9A), and then the purple suture is similarly

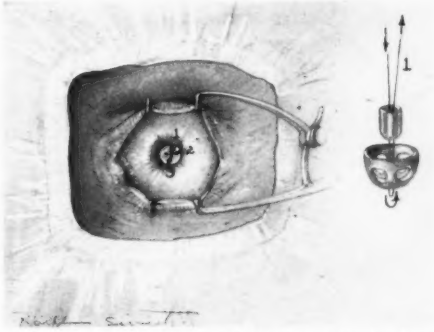

Fig. 10. Suture *1* pulled up, tied and cut, forcing button with Tenon's capsule and conjunctiva down into the basket.

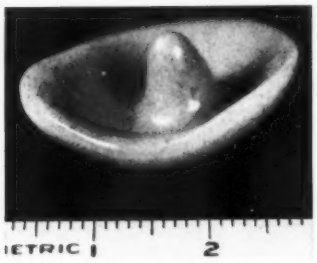

Fig. 11. Plastic retainer.

handled. This pulls Tenon's capsule and the conjunctiva into place and closes the opening.

A single tie is now placed in the black suture, and as this tie is gradually pulled up the index fingers make traction and a little pressure. The assistant then releases the button from the forceps. As this tie is pulled tight, it forces the button with Tenon's capsule and the conjunctiva down into the cup. Three knots are placed and the suture is cut (Fig. 10). No conjunctival sutures are necessary.

A lucite retainer is placed inside the lids. An adhesive dressing with firm pressure but with no roller bandage is applied.

POSTOPERATIVE COURSE

The first dressing is done on the third postoperative day, the retainer being removed and the socket irrigated. The retainer is replaced, and if there is still some edema an adhesive dressing is put back on for 2 more days. In most cases the dressing can be omitted. On the fifth postoperative day the sutures and the button are removed. A temporary retainer with button attached (Fig. 11) is placed in the socket at this time. This is removed daily, and the socket is irrigated for a week.

In none of the cases in which operation was performed has there been any prolapse of the conjunctiva. This is probably due to the type of operation and to the retainer. In general, there has been little reaction and no discomfort at all after the first postoperative day.

At the end of 2 to 3 weeks, depending on the shrinkage of its tissues, the socket is ready for a custom-made prosthesis, similar to the one shown in Figure 1.

COMPLICATIONS

It is important not to pull the sutures beyond the snug state, as otherwise pressure necrosis and exposure of the bottom of the basket will result. This complication will also occur if the button is not removed at the end of 5 days. If exposure of the bottom of the basket does occur, a retainer without a button attached is put in, and granulation and epithelization will take place in a few days, without impairment of the result. If, after the sutures and the button are removed on the fifth post-

Fig. 12. Appearance of socket in patient 1 month after operation, showing impression in the basket and the range of motion.

operative day, there is a thin-appearing lining on the bottom of the basket, a plain retainer can be used from 1 to 3 days and then a button retainer employed.

A sufficiently firm bite of Tenon's capsule must be obtained in placing the mattress sutures, since there is slight tension on the capsule when it is inverted into the basket. In 2 cases in which a ball implant was removed and a basket put in, the sutures did not hold. This was also true in a case in which a considerable amount of scar tissue was present—the sutures cut through the inelastic scar tissue. It was necessary in these 3 cases to remove the baskets.

Postoperative hemorrhage has never been a problem in our cases. In the 3 cases just mentioned, in which the sutures did not hold because of scar tissue and the basket was removed approximately 10 days after operation, it had to be dissected out. Certainly, the basket cannot be extruded.

PROSTHESIS

The socket is ready for the final prosthesis at the end of 2 or 3 weeks. This has been of plastic, made according to the standard Army procedure and under the direction of Captain Stanley F. Erpf and Captain Arthur L. Lundblad of the Dental Corps of the Army of the United States.

The prosthesis is not made from an impression of the socket, since that would result in its occupying too much of the available space. Figure 1 shows some variations in the prostheses that have been fitted. In general, the stud is adjusted to fit into the depression, and the base around this stud is cut away to allow the edge of the basket to come forward when the socket is turned. Through support of the stud, there is considerable relief of pressure on the tissues in the region of the fornices.

It is not absolutely necessary to use a custom-made eye with a stud; good movement can often be obtained with a Snellen form. The reason for this is that the movement of the prosthesis is in part due to the change in the shape of the socket when the basket rotates; one side becomes shallow and the opposite side deep, and the eye has to move.

The following tabulations were made on the basis of observations on 60 sockets fitted with artificial eyes. Practically all of them were fitted with custom-made plastic eyes. It is realized that this small number may not represent a true cross section. The series was collected from the wards without regard to the preoperative condition. It consisted of 20

Fig. 13. Patient 5 months after operation showing depression and movement of socket.

sockets without implants, 20 with ball implants and the first 20 with basket implants.

Average motion degrees	No implant	Ball implant	Basket implant
Nasally	19°	19°	28°
Temporally	13°	15°	22°
Superiorly	25°	20°	29°
Inferiorly	12°	20°	30°
Total	69°	74°	109°

The sockets without implants showed the greatest variation in movement from patient to patient and those with basket implants the least variation. This is illustrated by the following tabulation:

Prostheses having:	No implant	Ball implant	Basket implant
45° total horizontal movement	1 of 20	3 of 20	18 of 20
50° total vertical movement	6 of 20	8 of 20	19 of 20

These tabulations do not indicate the action of the oblique muscles, which is a prominent feature of the basket sockets. Neither do they indicate the most important characteristic of all, that is, the much more rapid response to movement of the muscle cone, with a notable decrease in the time lag as compared with that for the normal eye.

SUMMARY

On the basis of 100 operative procedures, a new type of basket implant for use after enucleation is presented which, with a new type of prosthesis, gives more instantaneous movement and a wider range of action. This procedure, combined with use of a plastic retainer, eliminates prolapse of implant and shortens the postoperative convalescence period.

RECONSTRUCTION OF ORBITAL FLOOR DEFECTS

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THE floor of the orbit is triangular in shape and is made up largely of the orbital plate of the maxilla. The orbital portion of the zygomatic bone makes up the anterolateral portion and a small portion of the posterior part of the floor is formed by the orbital process of the palatine bone. The anterior margin is thicker and stronger than the remainder of the floor. The inferior orbital fissure is the lateral boundary of the floor and the infraorbital sulcus runs forward along the central portion of the floor from the inferior orbital fissure to the infraorbital foramen, which lies about 1 centimeter below the lower orbital margin. The sulcus and foramen transmit the infraorbital artery and the main portion of the second division of the trigeminal nerve, that is the maxillary nerve, which is known as the infraorbital nerve as it passes into the infraorbital sulcus.

Trauma to the lower orbital margin with resulting fracture of the margin and floor of the orbit not infrequently produces more severe displacement of the thin floor of the orbit than of the thicker and stronger margin itself. The displacement of the floor is usually downward due to the concave orbital surface of the floor anteriorly and because an air space, the maxillary antrum, lies below the floor. It is Pfeiffer's opinion that fracture of the wall of the orbit is the entire cause for traumatic enophthalmos. Of 53 cases reported by him, 24 had a depressed fracture of the floor without any fracture of the orbital margin. More than half of these were caused by a blow with a fist. Pfeiffer states that "in the cases of less severe enophthalmos the posterior portion is fractured and in the cases of more severe displacement the entire floor is broken through." It is surprising how infrequent there is permanent visual damage in these cases. At times severe trauma to and fracture of the supraorbital area may produce an accompanying depressed fracture of the floor of the orbit due to transmission of the force through the orbital contents. Depressed fracture of the floor may also occur from the explosive force of shell fragments entering the orbit and from actual perforation of the floor by shell fragments or other foreign elements. It is quite unusual to have an elevation of the floor of the orbit unless there has been a severe crushing trauma to the region of the antrum.

A diagnosis of depressed fracture of the floor of the orbit is made on the history of trauma and the presence of depression of the eyeball with some enophthalmos. Diplopia may be present and also anesthesia or hypesthesia over the distribution of the infraorbital nerve. Immediately following the trauma these signs may be masked by edema and orbital hemorrhage. There may even be an initial exophthalmos. Crepitation from air in the soft tissues and palpable displacement of the orbital margin may be evident. Careful stereoscopic x-rays will usually confirm the diagnosis. There may be marked loss of vision due to internal ocular damage or due to compression of the optic nerve by fracture into the optic foramen or by hemorrhage into the optic nerve sheath in the foramen.

When there has been little or no depression of the floor of the orbit no treatment is indicated. When very definite depression is present it should be corrected as soon as the initial reaction has subsided. This is best done by the otolaryngologist by means of a Caldwell-Luc approach with elevation of the depressed orbital floor and moderate packing of the antrum for a day or two. When this is not done a permanent depression of the orbital floor and orbital contents results. Fracture and displacement of the lower orbital margin should also be corrected as early as possible, with internal wiring of the fragments or some method of external fixation, if necessary.

When there has been a severe compound comminuted fracture of the lower orbital margin it may be necessary to débride some of the

From the Surgical Service at O'Reilly General Hospital.
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Case 1.

Fig. 1. Appearance on admission.

Fig. 2. Final result.

Fig. 3. Wedge acrylic implant.

loose bone fragments. This results in more or less subsequent external deformity.

The purpose of any procedure to reconstruct the orbital floor is primarily to elevate the orbital contents. If sufficient correction of this depression is obtained it will also eliminate the sinking or retraction of the upper portion of the upper eyelid and lessen the enophthalmos. In late cases of depressed floor it is not possible to elevate the floor to its normal position because of the firm adhesions which have formed. In the past this has usually been accomplished by the use of autogenous or preserved cartilage grafts to the floor of the orbit, under the periorbita. This is the method used by most of the general plastic surgeons during the past few years in the army general hospitals that were ophthalmic and plastic centers. The taking of an autogenous rib cartilage graft makes an additional procedure, and at times the pleura has been accidentally perforated. The use of preserved cartilage has been quite satisfactory although it has been demonstrated that preserved cartilage buried subcutaneously produces a typical low-grade foreign body reaction over a period of months and is gradually absorbed and replaced by fibroblastic tissue. Osteoperiosteal grafts from the tibia have also been used. These are used to bridge the defect and usually require temporary additional support by packing in the antrum. This, together with taking of the graft, makes a needlessly complicated procedure.

It was our experience at O'Reilly General Hospital, and also the experience of ophthalmologists at some of the other army eye centers, that the use of various inorganic materials has been very satisfactory for orbital floor reconstruction with resulting simplification of the surgical procedure.

In June of 1945 at the suggestion of Dr. Reudemann of Cleveland, Lieutenant Colonel Struble at Crile General Hospital used tantalum wool and later tantalum mesh to fill in defects of the orbital floor in battle casualties in whom the Reudemann implant eye was being used. Struble stressed the importance of careful preoperative x-ray determination of the size of the defect, and received excellent cooperation from his roentgenologist, Lieutenant Colonel Shifflet.

During the latter months of 1945 Captain Souders of Dibble General Hospital used rhomboid shaped plates of the plastic acrylic (methyl methacrylate) to cover the defect of the floor of the orbit in old fracture cases who had some depression of the eyeball. Souders used various sizes and thicknesses of these acrylic plates depending on the amount of depression of the eyeball and size of the defect in the orbital floor. The dissection was made through a skin incision along the lower orbital margin but he placed the acrylic plate on the periorbita and not under it. The plate was held in position by sutures through small holes near the anterior edge of the plate and through the periorbita.

About this same time Major DeVoe of Halloran General Hospital used a packing of glass wool under the periorbita in several cases of depressed floor to fill in the defect and elevate the eye and orbital contents. He reported very satisfactory results and no complications.

In the spring of 1945 at O'Reilly General Hospital, we began to use a wedgeshaped acrylic implant to the floor of the orbit to elevate the orbital tissues in cases of anophthalmos who had had an enucleation with small implant in Tenon's capsule, or who had had a

Case 2.

Fig. 4. Appearance on admission. Fig. 5. Final result.

Case 3.

Fig. 6. Appearance on admission. Fig. 7. Final result.

simple evisceration of the eyeball. This procedure proved a quite satisfactory method to eliminate or lessen the retraction or sinking of the upper portion of the upper eyelid. We soon applied this procedure to cases of old fracture of the floor of the orbit with depression of the eyeball and enophthalmos. The acrylic wedges were made in 3 sizes, the average or middle size being about 2½ centimeters by 1½ centimeters and about 8 millimeters thick at one end and tapering down to about 4 millimeters at the other end. The operation is similar to that used by Gilles and others except that the wedgeshaped acrylic implant is used instead of a cartilage graft. After incision through the skin and subcutaneous tissue down to the lower orbital margin, the periosteum is incised and the periorbita thoroughly elevated with a submucous elevator. A wedge-shaped acrylic implant is then placed on the depressed floor with the thick end of the wedge posterior. A large enough implant is used to satisfactorily elevate the orbital contents and two or more implants can be used in cases of severe depression of the floor. Traction sutures in the tendons of the lateral and medial rectus muscle are a great aid in drawing the eyeball upward and forward at the time the wedge is being inserted. The periorbita is firmly closed with No. 000 gut mattress sutures. Subcutaneous sutures should also be used to avoid a depressed postoperative scar. A good pressure dressing is important to prevent or lessen hematoma.

Gilles was one of the first writers to recommend the use of cartilage grafts for replacing loss of bone of the orbital rim. This has been used extensively since that time. Lindemann in 1916 first described the use of an iliac bone graft to the mandible and this was later applied to the malar and infraorbital area by a number of plastic surgeons.

During the past few years tantalum plates, tantalum mesh, and acrylic plates have been used to replace loss of orbital margin. Too frequently the preformed tantalum or acrylic plate does not give the proper contour to the overlying tissues. It is difficult to alter these plates satisfactorily at operation. Also it is not a simple procedure to fashion the plate. Tantalum mesh is easily shaped at the operating table but it does not become firmly attached to the surrounding bone. Rib cartilage grafts do not become attached to the bone and also may change after operation. It was the experience of the eye and the plastic service at O'Reilly General Hospital that these inorganic materials and also cartilage grafts did not give as satisfactory results in reconstruction of the lower or lateral orbital margin, or malar area, as did the use of grafts of iliac bone. After removal of most of the cortex the cancellous bone can be easily shaped to fill in the defect properly and give a very satisfactory contour to the overlying tissues. If the ends of the graft rest on exposed bone it soon becomes firmly attached to this bone. A blood supply is rapidly formed into the grafted bone and a cortex or pseudocortex forms on the surface of the graft. Postoperative hematoma will seldom cause trouble if a narrow rubber

Case 4.

Fig. 8. Fig. 9.

Case 5.

Fig. 10. Appearance on admission. Fig. 11. After wedge acrylic implants. Fig. 12. Final result

tissue drain is used for 2 or 3 days after operation. This can be removed without disturbing the pressure dressing, and does not interfere with healing of the wound. The use of an iliac bone graft does add a procedure to the operation, but the final result makes it worthwhile.

Small defects of the lower orbital margin are satisfactorily corrected by the use of a fascia lata graft as advocated by Wheeler.

The following cases illustrate the satisfactory use of acrylic wedge implants to elevate the orbital contents in depressed fracture of the floor; also the use of cancellous bone from the ilium to reconstruct the orbital margin.

CASE 1. (Figs. 1, 2, 3) Patient incurred fracture of left lower orbital margin and floor of orbit with laceration of eyeball and lower eyelid from shell fragment. Enucleation with small implant in Tenon's capsule was performed 10 days later. He was later evacuated from overseas and admitted to O'Reilly General Hospital 3 months after injury. The lower eyelid was drawn down by scar tissue. Little deformity of lower orbital margin was present. He had been fitted with a large prosthesis in a large, retracted socket. There was obvious sinking of tissues below brow due to depression and retraction of orbital contents. Two months after admission a wedge acrylic implant was placed under the periorbita of the floor of the orbit. One month later a skin graft from the upper to lower eyelid with central lid adhesion was done. Lid adhesion was cut 3 months later and a new prosthesis made. Deformity is entirely corrected.

Case 6.

Fig. 13. Appearance on admission. Fig. 14. Before fitting of eye prosthesis.

CASE 2. (Figs. 4 and 5) Patient incurred fracture of left lower orbital margin and floor of orbit with destruction of eyeball from shell fragment. Enucleation without implant was performed the next day. He was admitted to O'Reilly General Hospital several months later. There was a slight depression of the malar area with faint overlying scar present. He had been fitted with a large eye prosthesis in a very deep, retracted socket. There was marked sinking of tissues below the brow. Three months after admission a grooved glass sphere implant was placed in the muscle cone behind Tenon's capsule. One month later the lower nasal side of the socket was enlarged with a mucous membrane graft. The lateral canthal ligament was transplanted 4 millimeters further temporal 1 month later. Three months following that a wedge acrylic implant was placed under the periorbita of the floor of the orbit. Following this he was fitted with a satisfactory eye prosthesis.

CASE 3. (Figs. 6 and 7) Patient incurred a fracture of the right lower orbital margin and floor of the orbit in an auto accident. Two months later there was obvious depression (5 millimeters) of the right eye with slight enophthalmos and retraction of tissues of upper portion of upper eyelid. The deformity was satisfactorily corrected by means of a wedge acrylic implant to the floor of the orbit.

CASE 4. (Figs. 8 and 9.) Patient incurred a fracture of the right lower orbital margin and floor of the orbit in a crash landing with subsequent persistent diplopia. He was admitted to O'Reilly General Hospital 6 months later. There was slight depression of the lateral lower orbital margin and malar area with the right eye about 5 millimeters lower than the left and 3 millimeters enophthalmic. There was slight weakness of the right superior rectus, internal rectus, and inferior oblique muscles. A wedge acrylic implant to the floor of the orbit gave a very satisfactory correction and eliminated the remaining diplopia so that he was returned to full duty.

Case 7.

Fig. 15. Appearance on admission. Fig. 16. Before bone graft. Fig. 17. Result.

CASE 5. (Figs. 10, 11, and 12.) Patient was struck in the right orbital area with a large stone and incurred severe compound depressed fracture of supraorbital area and of the floor of the orbit. Débridement of frontal sinus area and repair of lower eyelid performed at another general hospital. Admitted to O'Reilly General Hospital 3 months later. Severe enophthalmos and depression of right eye as well as marked depressed deformity of supraorbital area were present. He had loss of central vision due to traumatic damage to macular area. One month after admission the eye was quite well elevated and the enophthalmos fairly well reduced by means of five acrylic wedge implants to the depressed floor of the orbit. Recovery was uneventful. Two months later an iliac bone graft to the supraorbital area was performed by Lieutenant Colonel Karleen.

CASE 6. (Figs. 13 and 14.) Patient incurred a compound comminuted fracture of right zygoma and severe laceration of right eye from shell fragment wound. The right eye was enucleated 3 weeks later and 1 month following that a large cheek flap rotated to fill defect over zygoma region. He was admitted to O'Reilly General Hospital 6 weeks later. There was a long, broad, depressed scar from lateral lower orbital margin down to angle of jaw with loss of malar eminence and of lateral lower orbital margin. The lateral canthal area was drawn down about ½ centimeter. Three months later an iliac bone graft was used to reconstruct the lateral lower orbital margin and malar area, with excision of much of the scar. Two months later the lateral canthus was elevated by means of a Z-plasty or interposition of flaps.

CASE 7. (Figs. 15, 16, and 17.) Patient incurred severe compound comminuted fracture of right zygoma and maxilla with avulsion of lower eyelid and anterior segment of eyeball from shell fragment. The wound was débrided the same day. The eye was eviscerated 5 days later. He was admitted to O'Reilly General Hospital 1½ months later. There was a loss of entire right lower eyelid with conjunctiva and skin adherent to the remains of lower orbital margin. Due to fracture of the floor of the orbit there was marked depression of the orbital contents. Several operations were used to reconstruct the lower eyelid and the area of the lower orbital margin was reconstructed with an iliac bone graft. After the eyelid fissure was reopened the orbital contents were elevated by means of an acrylic wedge implant on the floor of the orbit. A fascia lata graft was used to correct the retraction below the brow.

SUMMARY

Fractures of the floor of the orbit should be reduced soon after injury, if feasible.

When late reconstruction is indicated the orbital contents can be very satisfactorily elevated by means of an acrylic implant on the depressed floor. Other materials such as tantalum mesh and glass wool have been satisfactory in the hands of some surgeons.

Small losses of the lower orbital margin can be satisfactorily filled by a fascia lata graft. Larger losses are best reconstructed by a graft of cancellous iliac bone with more consistently good results than cartilage grafts, or preformed tantalum or acrylic plates.

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THE RECONSTRUCTION OF THE UPPER LID

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WHEN considering this subject, "The Reconstruction of the Upper Lid", almost every person who has had experience with ophthalmic plastic surgery will immediately think of some more or less complicated case in the correction of which he had a part. The difficulties and complexities of such individual cases are most stimulating—of this there is no doubt. Nevertheless such cases, as all others, are corrected through certain basic principles peculiar to the subject, and common to all these conditions.

Regardless of any one technique, these principles can be divided into two major subdivisions—when reconstructing an upper lid is a good functioning eyeball present, and is the socket surgically anophthalmic? These two possibilities modify the surgery necessary to a tremendous degree.

A second group of three probable conditions which influence the necessary surgery, and contingent upon the first subdivision, are the eyelid defects themselves. First, is the deformity under treatment the result of the loss of the external layers of the lid only with normal conjunctiva present; second, in the case considered, are all the structures of the lid, both anterior and posterior surfaces, wanting, even partly; and third, are only the posterior lid surfaces and structures predominately deficient?

The presence of an intact functioning eyeball in lid reconstructions compels, without permissible modification, the use of conjunctiva or of mucous membrane for the reconstruction of the posterior surface of either lid. The absence of an eyeball, that is surgical anophthalmos, permits the use of epithelium either as a free skin graft or as some type of pedicle flap for replacing the lost posterior surface of the reconstructed lid. The reconstruction of a lid in cases in which no eyeball is present is a simpler procedure because demands are less exacting. Even the question of later lid motility is relatively insignificant, because corneal exposure and difficulties from that are not a problem. As a matter of fact, in many of these cases the ideal result hoped for is that of good-looking fixed lids which will retain a prosthesis satisfactorily even though they may be quite immobile.

A third consideration of importance in the reconstruction of a lid, especially the upper lid, is a thorough knowledge of the rather complex anatomy of this lid. Surgical principles which are harmonious with the anatomy of the upper lid are certain to give much better results than any technique which disregards this anatomy. One must remember that the lid has two major parts—a posterior conjunctival and tarsal plate surface or layer, and an anterior muscle and skin layer. The muscle pull of the levator palpebrae superioris is at a right angle to the muscle action of the orbicularis fibers. The two muscles lie in entirely different planes. These two muscles are not only antagonistic, one to the other, but both are very active muscles. Last, the two canthal angles are themselves quite immobile but here the two muscles have common attachments.

Reconstructive surgery for the correction of defects in the posterior surface of the lids is essentially the reconstruction of a cul-de-sac by means of mucous membrane. Cicatrices may be present, simultaneously, in the external surface of the lid, which needs reconstruction and resuture, but this is a minor part of the surgical procedure. A free graft of mucous membrane, sutured into a correcting position, is the basic essential (Fig. 1).

This same situation, when present with surgical anophthalmos, means a necessary correction either with the same type of graft or by means of a free skin razor cut graft. This must be cut as thin as is humanly possible. In these instances the external surface

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Fig. 1. Mucous membrane correction of the posterior surface of a defect of the lid.

Fig. 2. Simultaneous correction of posterior and anterior surfaces of the upper lid. Prosthesis in position.

Fig. 3. The major portion of the upper lid is lost with much cicatrix present. The entire superior cul-de-sac is absent. A pedicle flap from the forehead and a free skin graft to the posterior surface of the lid.

of the lid which is deficient, may be corrected simultaneously with either a pedicle flap or a free skin graft. Figure 2 is such a case. The superior cul-de-sac of the deficient socket was corrected by mobilizing the remains of the upper lid still present, swinging these inward upon themselves, as a hinged flap, to form the new posterior surface of a new lid. At the same time, the anterior surface of this lid was corrected with a free skin graft. It is in this type of case that the use of supraclavicular skin has such impressive successes. Figure 3 is a similar case, in which the correction of the external surface was achieved by means of a pedicle flap from the contiguous regions. A free razor cut epithelial graft was placed on the posterior surface of the lid flap. A pedicle flap had to be used here because of the extensive scar in the tissues remaining. To remove all of that meant the removal of almost the entire lid. In general, pedicle flaps are to be used only when necessary, never as an operation of election. When that is so, as in this indication, there need be no hesitancy about their use. If properly executed the additional scarring which they cause can be held to a minimum, often to an amount quite inconsequential. The value of a pedicle flap lies in the ability to transplant larger portions of epithelium under difficult circumstances, (anatomic, naturally) with a greater chance for continued viability in the graft than if that same amount of skin had been transplanted freely and without this added means for nutrition, i.e. the pedicle.

The ideal reconstruction of an upper lid in the presence of a normally functioning eyeball, assuming that both the anterior and the posterior surfaces of the lid have been lost in part, depends upon a technique originally advanced by Landolt in 1881, and subsequently carried to even greater general use by

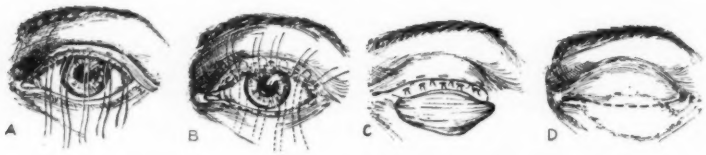

Fig. 4. Drawings modified after Axenfeld for an upper lid reconstruction.

Axenfeld in 1922, and by Dupuy-Dutemps in 1927. In more recent years, Hughes and McLean have given us beautiful demonstrations of the application of this technique, or its basic principles, in connection with malignancies of the lids. Figure 4 shows drawings modified from Axenfeld's description of the Landolt technique. The principles of the surgery depend upon the utilization of the lower lid for the reconstruction or repair of an upper lid.

For this technique, the lower lid is first split into its two basic layers. The lid margin is cleanly and wholly resected. The remains of the upper lid are similarly split into the two basic layers of the lid including all of the remnants of the lid. The margin of these layers is also resected, so that all four of these flaps have freshly bared edges to the margins. The remnants of the posterior layers of the upper lid and the posterior layer of the lower lid are sutured together, freshened edge to freshened edge, as a diaphragm across the eyeball. A small space is permitted to remain at the inner or the outer canthal angle for adequate normal lacrimal drainage. The lower lid skin and orbicularis is then sutured similarly, to the remnants of the external layer from the upper lid. The conjunctiva of the normal inferior culde-sac is almost sufficient for the complete replacement of the conjuctival surface of the upper lid, with enough in addition for a satisfactory inferior fornix. The skin surface of the lower lid, however, is quite insufficient. Because of that the lid surface of the lower lid must be incised throughout its entire length, and well undermined. The incision should be 4 to 6 millimeters from the former, now resected, lid margin. As the external skin surface of the lower lid is carried upward by the sutures just mentioned, this incision into the lower lid widens. It must be sufficient to release or permit an easy mobilization of the lower lid margin and a satisfactory suturing of this to the remnants of the upper lid. The defect caused in the skin surface is covered with a razor cut free skin graft, placed at the same time that the margins of the various layers are sutured. The tarsal plate of the lower lid will or should bridge the position of the former palpebral fissure.

After recovery from the above procedure that tarsorrhaphy across the front of the eyeball is incised, longitudinally, to form the new palpebral fissure. The two different layers of each of the new lids are carefully closed to

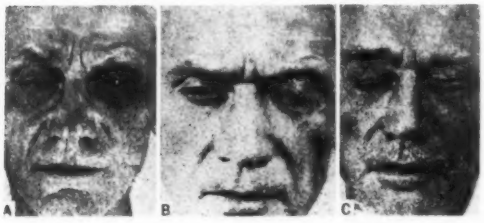

Fig. 5. A case corrected throughout with Axenfeld's technique. Notice the curve of the completed intermarginal tarsorrhaphy in B, showing the amount of tissue moved into the upper lid.

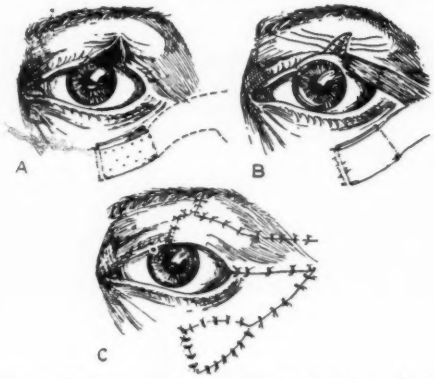

Fig. 6. Mucous membrane and epithelium for a simultaneous correction of a major defect in the upper lid.

Fig. 7. The complete correction of the upper and lower lids by an epithelial lined flap.

form a smooth lid margin. That tarsus which formerly lay in the lower lid will now lie in part, if not wholly, in the upper lid. The conjunctival surface of the two lids is usually quite adequate for good function. Figure 5 is an illustration of this technique. The entire upper lid was not lost but the major part was missing. The illustration in center shows the intermarginal attachments. The curve of that points out rather clearly the total amount of new tissue now lying into this position. The illustration at right shows the new palpebral fissure following its formation—also the degree of closure possible.

In this case the lashes were suggested by a line of tatoo marks at the new lid margin. A hair bearing graft for the eyelashes of the upper lid can be placed into position rather readily prior to the formation of the new palpebral fissure. Such a graft should be taken from the lower edge of the opposite eyebrow, cut with beveled edges, and sutured into position.

A second technique to be considered under similar circumstances, i.e., eyelid defect in the presence of a good functioning eyeball, necessitates the implantation of a mucous membrane graft into either the forehead or the upper lid immediately beneath the skin surface, to prepare the necessary graft with a posterior mucous membrane layer which will function as conjunctiva. This graft, either as a free graft or as a pedicle flap, is then transplanted to its correcting position for the simultaneous reconstruction of both the conjunctival and skin surfaces. Figure 6 shows the utilization of this basic principle by means of a pedicle flap, mucous membrane covers the posterior surface, and epithelium the anterior surface. Some of the principles of Wheeler's halving operation will apply in the utilization of this technique. This is so because those principles of Wheeler's are basic with ophthalmic plastic surgery whenever accurate carpentry is necessary in lid surgery. They are not characteristic of any individual procedure.

The mucous membrane to be used is taken from the buccal mucosa, trimmed to maximum thinness, wrapped over a mold, and then buried into a pocket prepared for it. After this has taken surgically, any portion of the mucous membrane may be transplanted with any amount of epithelium needed. In the instance shown a certain portion of the lid remains were rearranged and utilized by scar resection and by suture. The case was one of postmalignancy reconstruction. Somewhat less than one-half of the lid was still wanting following that. The mucous membrane epithelium pedicle flap was quite sufficient for a good correction. That portion of the rather conspicuous mucous membrane still present upon the skin of the lower lid had to be removed and the area covered with a skin graft. Skin from the supraclavicular region or from the opposite upper lid are equally satisfactory for this.

Hughes carried out this principle of combined mucous membrane epithelium graft by implanting the mucous membrane into a pocket of the opposite lid. Skin and mucous membrane were then transplanted as a free graft. Even though this technique was successful for the lower lid and perhaps should be

Fig. 8. An epithelial lined pocket on the face prior to transplantation for a new upper lid.

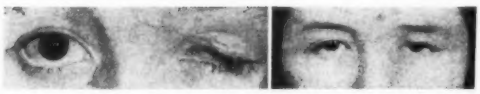

Fig. 9. A, left, Deformity of upper lid corrected by scar resection and resuture, also with a necessary enucleation. B, 3 months following surgery.

recommended for that, the use of a flap is better for an upper lid repair.

The complete correction, perhaps better expressed as correction for the more or less complete loss of an upper, a lower, or of both lids, in the absence of an eyeball, is similarly done but with epithelium rather than with mucous membrane. A pocket of epithelium is formed on the forehead or beneath the skin of the upper face. Following that one may transplant a flap having two epithelial surfaces, an anterior and a posterior surface, thus making possible correction for the complete loss of one or more lids. The principle is quite like that described in detail for the use of mucous membrane but the absence of an eyeball permits the use of epithelium for the posterior surface of the new lids. Figure 7 illustrates such a case before and after its correction. Figure 8 shows a pocket upon the face before transplantation to an upper lid.

In this presentation the only cases considered for the explanation of the rules for lid reconstruction were those in which there had been a loss of soft tissue to such an extent that the replacement of these tissues was necessary for the correction of the case. Many cases could be presented wherein the correction was obtained by simple (meaning uncomplicated and not ease of performance) scar resection, resuture and the reposition of those tissues still present, to correct the plastic defect present. Figure 9 is such a case. The necessary enucleation of the phthisical eye had little effect upon the condition of the lid. Scar removal and suture were responsible for the satisfactory result obtained. This possibility as a surgical principle must be remembered in the consideration of cases for correction. It is properly included herein considering the title of the paper and the scope of its subject matter.

Fig. 10. A, left, Extensive ectropion following herpes, the lids opened and closed. B, Correction with a razor cut free skin graft.

RECAPITULATION AND CONCLUSION

In this presentation, such defects as ectropion, entropion, symblepharon, etc., have not been the basic conditions under consideration. The extent of pathology possible in some of these conditions, however, as illustrated in Figure 10, might permit one to consider this degree of deformity worthy of the term—lid reconstruction. It is, nevertheless, only a case of extensive ectropion and as such is to be corrected by procedures rather well established for this type of condition.

The real purpose of the paper has been to outline the principles underlying lid reconstructions, and especially when applied to the upper lid. The different anatomic possibilities which present themselves for correction differ so decidedly in their demands and hence in the permissible surgical techniques available for correction that it was thought necessary to emphasize again that basic fact.

These surgical principles, as they have just been discussed, are the result of clinical experience, and as such they should be seriously considered as these cases appear for correction.

THE MANAGEMENT OF NONMAGNETIC INTRAOCULAR FOREIGN BODIES

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THE character of intraocular foreign bodies coming to the ophthalmic surgeon's attention has changed materially in recent years. Formerly 95 to 98 per cent were magnetic, leaving a bare 2 to 5 per cent of cases to which the magnet was not applicable. Now some series of cases are reported in which the nonmagnetic percentage runs as high as 10 and even 40 per cent.

The ratio of nonmagnetic to magnetic intraocular foreign bodies was always higher in battle casualties than in civilian life. This ratio took a sharp rise with the nefarious introduction by the Axis forces of nondetectable, nonmagnetic land mines in the North African Desert campaigns as reported by Stallard (16). The World War II experience of the United States Army Medical Corps is well described in Wilder's report, that out of 150 enucleated eyes received at the Army Institute of Pathology, 89 harbored nonmagnetic particles.

The increased use of alloys containing copper, aluminum, brass, lead, zinc, manganese, nickel, etc., in industry as well as war thus presents new and difficult problems. In addition to these one runs across eyes harboring glass, plastics, coal, stone, sand, lashes, grit, wood, and other substances.

Our miracle tool the magnet is worthless in application to nonmagnetic substances. Nor, does it attract steel alloys containing considerable manganese. Often the ophthalmologist was thus made to despair on seeing a patient with a nonmagnetic intraocular foreign body. New simplified and improved x-ray and other localization methods with improved surgical techniques have made it possible to save some of these eyes from blindness. Several problems present themselves when one is called to attend a traumatized eye:

1. How shall one proceed in the average case of ocular injury?

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2. When should an intraocular foreign body be suspected?

3. How much damage has been done to vital structure?

4. Is a foreign body present within the eye and how can we readily localize it accurately?

5. How does one differentiate the nonmagnetic from the magnetic foreign body.

6. To what extent does infection complicate the picture and how shall we control it?

HISTORY

The ophthalmologist should investigate the possible presence of an intraocular body in every case of possible injury and especially in uveitis. The history is most important. The examiner must question the patient in detail about the likelihood of exposure to injury while hammering, chiseling, or working with rotating or moving machinery. One should note whether the patient was near flying particles or near an explosion or in proximity to shattering solids. An investigation of the tools and substances in use at the time of accident gives a clue as to the likelihood of the intraocular particle being magnetic or otherwise. It also may tell us whether the fragments are glass, or stone, or copper, or steel, etc.

Stallard (16) writing of his North African war experiences found a clue to the nature of the intraocular fragments by examining small particles lodged in the skin of the lids and face. U. S. Army ophthalmologists have examined injured eyes which contained more than one particle, some magnetic and others nonmagnetic. Close questioning of the patient may further reveal the size of the fragment and its course of flight toward the eye. The lapse of time since injury is necessary to ascertain. Fragments that have been in contact with soil may harbor tetanus bacilli. These and a host of other details may be elicited by a careful history. Previous "negative" examinations, or the story of removal of a superficial corneal

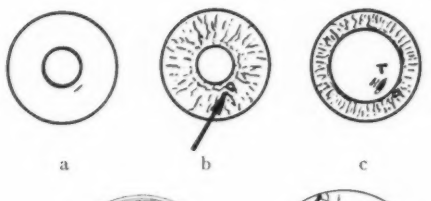


Fig. 1. Course of foreign body through the globe and trauma caused to a, cornea (perforation), b, iris (arrow points to hole), c, lens (tract through it). d, Section of globe showing tract of particle, location of foreign body and vitreous opacities due to hemorrhage. e, Foreign body lodged in retina, as viewed with ophthalmoscope.

particle should not lead us astray. There are many cases on record dismissed with a pat on the shoulder, which later turn up with siderosis or chalcosis or a cyclitis due to an intraocular foreign body.

THE EXAMINATION

Both eyes must be examined subjectively and objectively. One may find evidence of disease, of injury or even of sympathetic ophthalmia. Visual acuity and field examination of each eye, where possible, should be followed by complete examination with all the instruments and methods at our command. The anterior segment must be studied with loupe and oblique illumination, with ophthalmoscope, with the transilluminator and particularly with the slit-lamp microscope. The cornea, the conjunctiva, the sclera, the anterior chamber, the iris, the lens, the vitreous, the entire visible retina and the optic nerve must be painstakingly scrutinized. If photophobia or pain interfere, a drop of local anesthesia such as tetracain 0.5 per cent may facilitate the examination. A perforating wound in the cornea as evidenced by a hole in Bowman's and especially in Descemet's membrane leaves permanent telltale evidence. A hole in Descemet's membrane or in the iris leaves permanent evidence. Discovery of such, however minute, is proof of a penetrating wound and charges the examiner with an exhaustive study to establish the presence of an intraocular foreign body and to localize that foreign body.

The value of exhaustive routine examination is evident from the next 2 cases cited:

CASE 1. A.T., mechanic, aged 30 years, complained of occasional discomfort and redness of the left eye. Routine examination revealed a minute perforation of Descemet's membrane. A history of injury 6 months previous while chiseling was finally elicited. The patient remembered that a foreign body was removed from the conjunctiva by a fellow workman. Since then his eye watered in bright light, etc. The first x-ray examination was negative. A second x-ray examination by Vogt's soft tissue technique revealed a minute fragment near the iris root. With the aid of gonioscopy it was possible to visualize the foreign body covered by exudate in the lower anterior chamber angle. The particle was subsequently removed and the eye quieted down.

CASE 2. J.B., Auto repairman, aged 34 years, referred with 24 hour old perforation of his left eye by a piece of wire. Examination revealed a left corneal perforation in the pupil zone with swollen traumatic cataract bulging into the anterior chamber.

Vision of the right eye was 20/25. Slit-lamp examination of that eye revealed early siderosis and a healed limbus perforation. X-ray examination of both eyes located a small irregular metal splinter in the right ciliary body. The left eye was negative roentgenologically.

Further questioning revealed a history of injury 9 months previous while working on another job. The first aid attendant and the plant surgeon found no foreign body at that time and since there was no pain and very little redness the eye was dismissed as negative at that time.

The examination gave evidence of 2 distinct injuries involving both eyes: the fresh perforation of the left eye without foreign body, a forgotten injury of the right eye (proved to harbor a small steel splinter). A magnet extraction was performed by the anterior route on the right eye. The left eye was atropinized and watched for several days after which a linear cataract extraction was performed.

ROENTGENOGRAPHY AND LOCALIZATION

With the clinical examination completed one proceeds to x-ray examination and localization. Accurate localization is the *sine qua non* for the proper management of intraocular foreign bodies. It is best to look up a roentgenologist who takes special interest in foreign body localization. It is good policy for the ophthalmologist to be thoroughly familiar with x-ray foreign body localization. He should be

able to supervise the localization and he should be able to suggest variations in the technique so as to determine whether a fragment is in, or just outside, the eyeball. Glass (unless containing lead), wood, and many other substances are not opaque to x-rays. Metallic and stone splinters are x-ray opaque. But a minute foreign body can be overlooked. Sometimes artefact shadows are produced by imperfect screens. Because of this it has been our practice to advise first qualitative study by (a) stereo-x-ray in posteroanterior view with patient's chin and nose resting on the x-ray cassette, (b) lateral stereo of the affected eye, (c) skeleton free (soft tissue) technique of Vogt (28, 29) for minute fragments in the anterior segment (see Figs. 1, 2). The latter is performed by pressing the corner edge of a dental film into the inner canthus and shooting across from the temporal side with the central x-ray beam (soft ray). This can be done with the eye looking successively in various directions, namely, up, straight ahead, down, abducted, and adducted as necessary. This exposes all portions of the anterior segment. The eyelids may be pulled out of the way by adhesive strips. A small metal marker attached to the upper and lower limbus at 12 and 6 o'clock helps orientation. Proptosis, produced by injecting retrobulbarly 2 to 4 cubic centimeters of 2 per cent procaine, aids in exposing more of the globe to this skeleton free soft tissue technique. Thus, some substances, such as glass or minute metal splinters, which would be obscured by bone shadows and would not show up by the usual technique, become visible by Vogt's method.

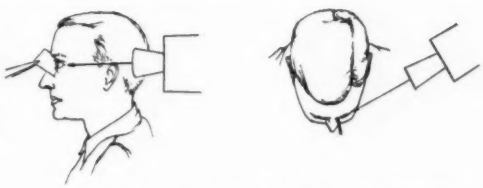


Fig. 2. Vogt's skeleton-free x-ray technique for localization of foreign bodies in the anterior segment of the globe. Plate tube distance 30 inches equals 75 centimeters.

Localization is readily performed by Comberg's method (2, 12). This method is simple and accurate when properly applied. It is foolproof for it indicates automatically, voluntary, or involuntary rotation of the eyeball away from the desired position.

A drop of 0.5 per cent pontocaine is instilled in the conjunctival sac.

A contact lens with 4 lead markers on the limbal sclera is inserted beneath the eyelids so that the raised portion fits over the cornea. The lens is rotated so that the lead markers are at, or nearly at, the 3, 6, 9, and 12 o'clock meridians.

First a posteroanterior exposure is made with the patient in prone position (chin and nose resting on casette to throw the petrous pyramid shadow below the orbit) (Figs. 4, 6). The patient looks straight ahead so as to see a reflection of his uninjured eye in the casette, or in a small pocket mirror lying on the casette before the uninjured eye (Fig. 4a). The central ray (perpendicular to the plate) is aligned with the anteroposterior (visual) axis of the globe. In the presence of strabismus, a thin

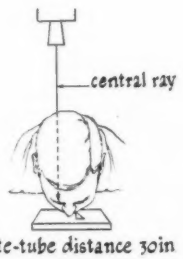


Fig. 3.

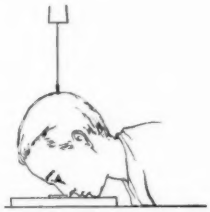


Fig. 4.

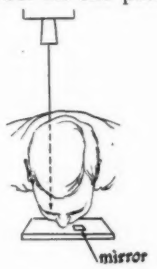


Fig. 4a.

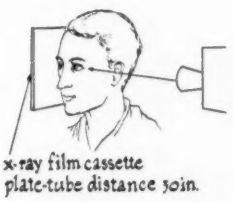


Fig. 5.

Figs. 3, 4, 4a, 5. Modified Comberg localization technique with contact lens. Central ray is over the injured eye.

Figures 3, 4, and 4a show method of taking posteroanterior exposure in chin-nose position. Uninjured eye looks into fixation mirror. Figure 5 shows method of lateral exposure. Injured eye is next to plate. Central ray passes through limbus. Plate tube distance 30.

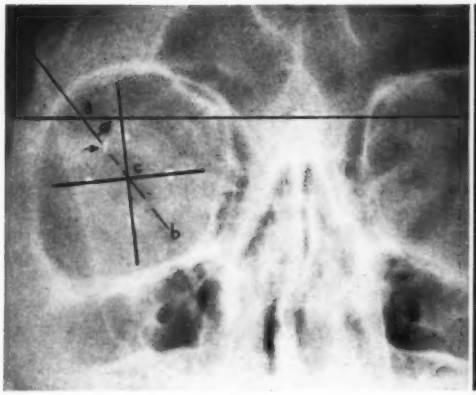


Fig. 6.

Fig. 7.

Fig. 6. X-ray localization posteroanterior view (chinnose position: petrous pyramid projected below orbit). Contact lens with lead markers in position. Foreign body is shown by arrow. *c* is corneal center located by drawing diagonals between markers. Line *ab* drawn through foreign body and corneal center makes angle ϕ with horizontal orbit line.

Fig. 7. X-ray localization lateral exposure. Glass localizing contact lens with lead markers resting on globe. Arrow marks foreign body. Measurements along line *cd* gives distance of particle behind limbus. Correction factor due to x-ray distortion in Figures 6 and 7 is 10 per cent.

cover glass mounted on a black cardboard triangular wedge is used as an angle mirror to reflect a pocket flash light into the noninjured left fixating eye (Fig. 3). The light is held so that the visual axis of the injured right eye is perpendicular to the x-ray plate. The central ray must pass coaxially with the visual line of the injured eye. If one eyed, the patient is instructed to look at the reflection of his eye in the polished cassette surface. If this is not possible due to low visual acuity, the angled cardboard mirror and flash light are employed before the only eye. Then a lateral exposure is made with the patient lying on the affected side and looking straight ahead at a mark on the opposite wall. The central ray should pass through the limbal plane bisecting the cornea (Figs. 5, 7).

The measurements taken from the posteroanterior and lateral views are corrected for distortion by reducing them by 10 per cent. They are then plotted on Comberg's localization chart (Fig. 8). In the posteroanterior view (Fig. 6) the lead dot shadows are connected diagonally by lines scratched on the x-ray plate to give the center of the cornea. A line, *ab*, drawn through the foreign body and the corneal center, *c*, makes angle ϕ, with a line drawn parallel with the roofs of both orbits. The angle is measured with a protractor and transferred to the localization chart (Fig. 8)—and is shown to correspond with the 120 degree meridian. The distance from foreign body to visual axis on x-ray plate (Fig. 6) corrected for x-ray distortion by 10 per cent is plotted on this circular front view.

From the lateral exposure (Fig. 7) one determines the distance of the foreign body from the limbal plane along the line, *cd*. The anterior and posterior limits, 13.8 millimeters and 16.6 millimeters respectively, are plotted on the meridional section of the eye through the 120 degree meridian. The radial distance—foreign body to posteroanterior axis—is taken from (Fig. 6) as plotted on (Fig. 8a) and is again plotted on (Fig. 8b). This corresponds with its position in the upper temporal quadrant of the posterior vitreous. One can readily realize that a movement of the globe would be shown by a corresponding change in position of the localizing shell. (Figs. 6 and 7 show exposures with a glass contact lens.)

There are several objections to the Comberg contact lens. It does not always lie centered on the cornea and being made of glass can break on falling.

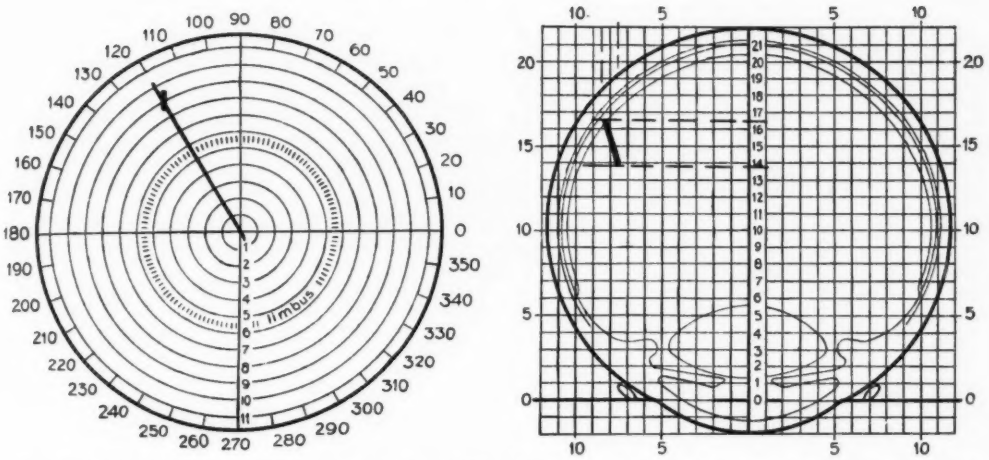


Fig. 8. Localization diagram at left, a, front view, denotes meridian. At right, b, location of fragment in plane of 120 degrees meridional section.

Since 1941 (19) the writer has often used an acrylic localizing shell similar to Comberg's contact lens. We modified the Comberg lens (20) in 1944 by having 3 suture holes drilled at 3, 6, and 9 o'clock near the lens edge (Fig. 9). It can thus be anchored to the episclera with 3 silk sutures. This does away with shifting of the localizing shell on the globe by lid pressure or by gravity (as happens in some cases). A vent hole was drilled near the limbus in the corneal portion to permit easy removal of the lens and avoid suction adherence which might traumatize a freshly injured eye. The glass lens may be sterilized with 70 per cent alcohol. The plastic lenses are sterilized in 0.1 per cent mercury oxycyanide. The plastic lens is applicable to localization only.

For visualizing the anterior segment of the globe stereoscopically (19), and for a true concept of the topographic position of the foreign body, the glass lens is most useful because it is visible in the film. When viewed in the stereoscope in lateral and also posteroanterior views, it affords an excellent tridimensional concept. This is further enhanced by completing the scleral arc on the film with a sharp pointed compass. Then one has the quite realistic illusion (21) of seeing the foreign body in relation to the walls of the globe. Spaeth and others have found the suturing a small ring marker to the sclera near the localized foreign body especially useful during surgery.

Brigadier Graham (17) sewed a thin silver wire ring 12 millimeters in diameter at the corneal limbus for x-ray localization. This method was followed by Stallard in North Africa. Sweet's method for x-ray localization is quite accurate but requires special apparatus and has no check on movement of the patient's eye. Comberg's method here described is simple and accurate.

For outlining the globe in suspected double perforation, air injection in Tenon's space was reported by Gasteiger and Grauer in 1929, and by Spackman in 1932. Stereoscopic roentgenograms are then made. We have found this method satisfactory for establishing that a foreign body has traversed the globe and lodged in the posterior orbit. Further information may be gained in using the above air study by applying a Comberg glass localizing shell to the cornea as suggested and used by the writer since 1942.

MAGNETIC AND INDUCTION LOCATORS

Some surgeons have advocated the application of the magnet to the injured eye to determine whether the intraocular foreign body is magnetic. This is to be deplored, since considerable damage to the ocular structures can

be done by such methods. Nor, are such tests conclusive. The magnet should be applied only in the operating room and then only after x-ray localization. The sideroscope was in use in the latter part of the 19th century to determine the magnetic character of foreign bodies. It was unreliable and fell into disuse.

Since 1943, I found the Berman locator especially valuable in determining whether an intraocular foreign body is magnetic or nonmagnetic. It has been useful in locating and pinpointing the spot on the sclera closest to the magnetic fragment. It has served as a check on x-ray localization (which is usually correct and occasionally faulty). It has made possible the determination as to whether the fragment has actually moved after magnet application. It has helped me to decide whether the giant magnet or the hand magnet was necessary for extraction of a foreign body. It has served as a psychological comfort throughout the operative procedure. It was first used by Moorhead at Pearl Harbor in 1941. Minsky published the first recorded application of the locator for the transscleral removal of an intraocular foreign body. So far, it has not aided in localizing small nonmagnetic fragments.

JUDGMENT AS TO PROCEDURE

Having determined the character and having localized the foreign body, having determined the absence, or presence and extent of infection, having arrived at some conclusions as to the amount of ocular trauma and having come to the conclusion that some measure of vision can be saved, one asks himself, "which foreign bodies should be removed and which might best be left undisturbed?"

Chemically inert substances such as glass and stainless steel do not cause ocular irritation as a rule. Aluminum is also well tolerated. On the other hand, brass, copper, zinc and their alloys, iron and steel produce ocular inflammation and deterioration. One must use careful considerate judgment in deciding on operative interference.

Prompt removal of an intraocular foreign body before it sets up too much irritation or infection and before it becomes surrounded by exudate is essential. It is wise to attempt the removal of all irritating nonmagnetic foreign bodies, if one can avoid excessive mutilation of the globe in doing so. Prompt and early survey followed by a well considered plan of procedure should be the rule. The surgeon with all facts at hand, decides whether operative interference or conservative treatment is to be followed. Should surgery seriously threaten the integrity of the eyeball and prove to be mutilating or destructive, then one must realize that nothing is to be gained by performing an operation.

COMBATING INFECTION—PROPHYLAXIS

Every early foreign body case, when first seen, must be considered as potentially infected. To combat such infection, and before any organism can be isolated, the surgeon must rely on prophylactic measures. Since the days of Wagner-Jauregg's malaria treatment of syphilis, ophthalmologists have found that foreign protein therapy, in the form of 15 to 30 million typhoid bacilli antigen intravenously or 10 cubic centimeters of boiled milk intragluteally, are helpful in controlling intraocular inflammation. On admission 1500 units of antitetanic serum is given. Penicillin—100,000 units—is given intramuscularly as an initial dose and is repeated in 50,000 unit doses every 3 hours for 4 to 6 days. We have also found subconjunctival injection of 500 units of penicillin dissolved in 0.5 cubic centimeter normal saline to be helpful.

Sulfadiazine has been especially valuable in our experience in combating infection. Six grams are given during the first 24 hours beginning with a 2 gram dose. Four grams are then given daily in divided doses for another 48 hours. Thereafter, 2 grams are given every 24 hours for 5 days. A blood level of 8 to 10 milligrams is desirable. The urine must be watched for sulfa crystals. The blood must be watched for leukopenia and anemia.

PREOPERATIVE CARE

As preparation for local anesthesia, pentobarbital 0.1 gram is given 1 hour before operation. The skin is scrubbed with soap, irrigated and painted with 3½ per cent tincture of iodine or merthiolate.

Local anesthesia is performed in the following manner.

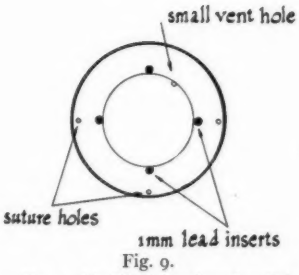


Fig. 9.

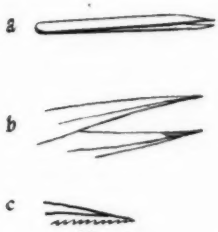


Fig. 10.

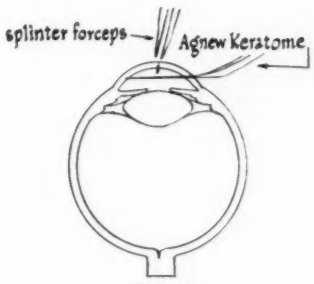


Fig. 11.

Fig. 9. Modified Comberg localizing shell made of plastic or glass. It may be anchored to episclera at 3 suture holes.

Fig. 10. Author's corneal splinter forceps. a, General view of entire forceps, b, enlarged view showing sharp points and serrations on blade, c, lateral view illustrating backward pointing serrations. They afford a strong grasp.

Fig. 11. Kuhnt's method of removing penetrating corneal splinter, pupil zone, aided by use of forceps.

1. Pontocaine hydrochloride 0.5 per cent is instilled topically 3 drops at 1 minute intervals.

2. Procaine 2 per cent with 1:30,000 epinephrine is injected into the lateral canthus, subconjunctivally and into the superior rectus tendon.

3. Akinesia is performed by injecting 5 cubic centimeters of 2 per cent procaine, containing 1 minim of 1:1000 epinephrine 10 to 15 millimeters anterior to the incisura intertragica (ear notch).

4. Retrobulbar injection consists of 0.5 cubic centimeter solution, containing cocaine hydrochloride 1 per cent, procaine 2 per cent, epinephrine 1:30,000.[1]

CORNEAL FOREIGN BODIES

Superficial foreign bodies may be wiped off with a moistened cotton applicator after topical anesthesia. Imbedded particles are dislodged with a sharp spud used to pry up the edge of the fragment. Multiple imbedded foreign bodies are readily removed with the 1 millimeter curet.

The narrow beam of the slit-lamp microscope is invaluable in ascertaining the depth of a corneal foreign body. It readily affords information as to whether a particle is wholly intracorneal or projects into the anterior chamber. Metallic slivers, or wooden splinters between the corneal lamellae, are removed by dissecting down on them and then prying them up with a cataract knife. When somewhat dislodged the splinter is grasped with the author's corneal splinter forceps (22) (Fig. 10). This forceps has fine rasped teeth which point backward and provide an excellent hold. Thorns and wood splinters are likely to cause keratitis if removed incompletely. On the other hand, small glass spicules, or coal particles, or powder particles if wholly intracorneal may be left undisturbed since they rarely irritate.

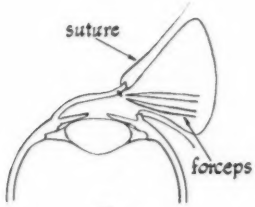
The more troublesome corneal foreign bodies are the ones penetrating to or into the anterior chamber. There is always danger of pushing them into the chamber; also the hazard of producing traumatic cataract if the projecting fragment strikes the lens capsule.

Penetrating corneal foreign bodies in the pupillary zone are best removed by the method suggested by Kuhnt many years ago (Fig. 11). Pilocarpine is used to contract the pupil. A narrow keratome (4 mm. wide) such as that of Agnew or of Castroviejo is introduced through the cornea and the point anchored on the other side. The keratome blade thus lies beneath the foreign body. One now dissects the corneal layers down to the foreign body and removes the fragment with the splinter forceps. The keratome is now withdrawn and the pupil is dilated with atropine. The anterior chamber is restored with normal saline to avoid anterior iris synechia.

A penetrating splinter in the periphery is removed after making a corneal flap, inserting 1 or 2 interrupted sutures (Fig. 12). The flap is lifted and the foreign body is removed with

[1]To prepare procaine 2% with 1:30,000 epinephrine, add 1 minim of 1:1000 epinephrine solution to 2 c.c. of 2% procaine solution.

Fig. 12.



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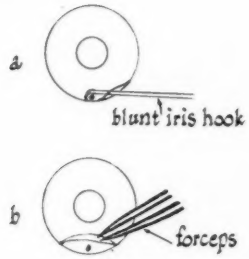

Fig. 14.

Fig. 12. Limbal incision and preplaced sutures for removing peripheral placed penetrating corneal splinter.

Fig. 13. Second step in removal of splinter from everted cornea with forceps.

Fig. 14. a, Use of blunt iris hook to dislodge fragment wedged in chamber angle. Final removal with forceps. b, Forward incision in cornea permitting access into chamber angle.

forceps from within (Fig. 13). It may be necessary to pry the splinter loose with a knife needle.

Another method for removing deep corneal foreign bodies is to make pressure from inside, with a small Reverdin needle (inserted through a keratome incision) against the posterior surface of the cornea while cutting down onto the foreign body (Fig. 15).

FOREIGN BODIES IN THE ANTERIOR CHAMBER

Magnetic particles in the anterior chamber rarely require the insertion of an instrument into the globe, except for toilet of the wound. On the other hand, the nonmagnetic fragment must depend on special forceps, a blunt iris hook, and an Elschnig spatula for its removal. Small particles of glass, coal, inert solids, and rootless lashes do not as a rule require surgery. Copper and brass must be removed.

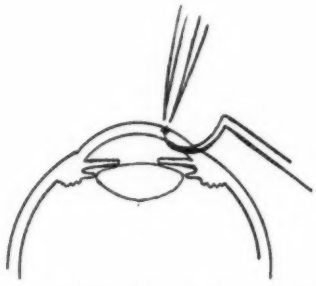

Fig. 15. Use of Reverdin needle through keratome incision to press foreign body backward through cornea while extraction is attempted from without.

It has been our practice to use the Berman locator in every case, and on occasion we found an intraocular foreign body to be magnetic, when the history suggested otherwise. The penetrating corneal foreign body is at times pushed into the anterior chamber and then it is obviously handled as such.

For the operation one should have at hand the usual iridectomy instruments, plus: serrated curved anterior chamber clot forceps, Arruga's capsule forceps, the author's corneal splinter forceps, Tyrrel's blunt iris hook, Elschnig's cyclodialysis spatula, and an anterior chamber irrigator. It should be a rule to fill the anterior chamber with normal saline at the end of the operation. Hyphema should be allowed to absorb or must be irrigated away before removal can be attempted.

Nonmagnetic foreign bodies not enmeshed in iris tissue are readily grasped and removed with one of the above special forceps through a properly placed keratotomy. It is best to avoid the wound of entry unless it is large. The corneal incision should be posterior to the foreign body so that the rear wound lip will not interfere with instrumentation. The particle should be grasped so that it will not dart away. The lens capsule must be avoided. After removal of the fragment, any iris prolapse that may be present is replaced, the chamber is then restored with saline and in most cases it is advisable to close the incision with atraumatic silk sutures. This prevents postoperative iris prolapse. No atropine is instilled at this time. A binocular occlusive dressing is applied. After 3 or 4 days, 2 per

cent atropine is instilled. Both eyes are kept closed for 1 week if the incision is longer than 6 millimeters.

Anterior chamber foreign bodies of long standing, either adherent or enmeshed in iris tissue may at times be teased loose. They usually require an iridectomy. Only the smallest amount of iris tissue should be sacrificed.

ANTERIOR CHAMBER ANGLE

Nonmagnetic particles lodged in the chamber angle present a special problem. Most of them are found in the lower angle recess due to gravity. They are usually wedged between iris and cornea and are often covered by exudate. They may be readily seen by gonioscopy. Removal may be accomplished by a method long in use. A limbal incision is made several millimeters to the side of the particle (Fig. 14a). The fragment is pried loose with a blunt iris hook and is then removed with forceps. The incision is then closed with silk sutures and the anterior chamber is reestablished with normal saline.

Desmarres in 1874, Goulden in 1920 and Lancaster later described another good approach to particles lodged in the anterior chamber angle. An incision is made from within forward across the cornea from 5 to 7 o'clock with a narrow Graefe cataract knife (Fig. 14b). This permits one to pry the foreign body loose with the blunt hook and then to reach in with forceps and remove it. The chamber is restored and the corneal wound is closed with one or two interrupted sutures. Both of the above methods have been tried several times and found satisfactory by the writer.

It may at times be necessary to incise the angle from without (*ab externo*—according to the method of Gayet). Or one can use Meller's method of making a hinged trephine button over the site of the foreign body. Here one must be certain not to have a corneal shelf overlying the fragment in the chamber angle.

IRIS

Nonmagnetic particles lodged in iris tissue can at times be freed with forceps inserted through a keratotomy. However, when it is firmly enmeshed or when the iris is excessively traumatized in removing the splinter I have found it best to excise a small portion of iris with the foreign body.

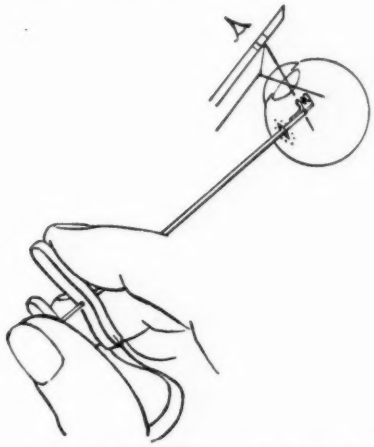

Fig. 16. Method of using author's self-closing vitreous foreign body forceps under ophthalmoscopic control.

POSTERIOR AQUEOUS CHAMBER

To remove foreign bodies from behind the iris just to the side of the lens equator, one must have extremely accurate x-ray localization with contact lens or limbus marker. A Gayet incision is made subconjunctivally (beneath a previously dissected flap) with Lundsgaard's knife. A McLean corneoscleral suture is then placed and the incision is completed *ab externo* into the chamber angle. A drop of adrenalin 1:100 and a drop of thrombin solution are placed on the iris root to prevent and arrest hemorrhage. Iridodialysis at the root is accomplished by holding the iris up and cutting it at its attachment with pointed scissors under Beebe loupe magnification. The iris is now held aside while the corneal flap is lifted by the assistant. The surgeon reaches in with forceps, grasps the foreign body and removes it. The fragment if present for any length of time may be enmeshed in exudate. One must be extremely careful to avoid lens injury. The incision is closed with the above mentioned suture. A thin strand of iris stroma may be incarcerated in the wound just before closure if the iridodialysis is longer than 3 millimeters. The conjunctival flap may be replaced and held with 2 interrupted silk sutures.

FOREIGN BODIES IN THE LENS

Nonmagnetic foreign bodies are sometimes tolerated by the lens for long periods of time because of its slow metabolism. They may thus be carried along until the lens becomes completely cataractous. For removal of lenticular foreign bodies the pupil must be dilated maximally. Magnetic splinters are readily dislodged with Haab's giant magnet from either partly or wholly cataractous lenses.

To remove visible nonmagnetic splinters from the lens, Donovan in 1925 suggested a unique method. A small keratotomy is made and a short beveled 19 gauge hypodermic needle mounted on a Luer syringe is inserted into the lens up to the foreign body. The plunger is pulled on to grasp and hold the foreign particle by suction. Donovan has reported successful extraction of several lenticular foreign bodies by this method.

If the fragment lies just beneath the anterior capsule, it may be grasped with a toothed capsule forceps.

The customary practice with foreign bodies in the lens (without irritation of the eye) is to await complete maturity of the cataract. Combined intracapsular extraction is then attempted. In adults under 40, the Pagenstecher technique (of holding a Weber loop or broad spatula just behind the superior lens equator while counter pressure is made at the lower limbus) is employed. Vitreous loss is kept at a minimum by tying previously inserted corneoscleral sutures. In patients past 40 years of age, one tries to remove the lens in capsule using Arruga's forceps or the erisiphake. Rupture of the capsule with escape of the foreign body can present a serious complication. If it is visible, one can grasp it with forceps. If it is not seen readily, then one applies the scleral transilluminator gently to the globe in an attempt to see the foreign body shadow. The cataractous nucleus is expressed. Irrigation, under Beebe loupe control, is resorted to to float the foreign body into view.

NONMAGNETIC FOREIGN BODY IN CORPUS CILIARIS OR CHORIOID

Accurate localization is essential. A ring marker sewn to the episclera is helpful. The conjunctiva is incised several millimeters behind the localized spot and the sclera is bared over this area. The exact spot of localization is marked with gentian violet. A meridional incision is made through the sclera by gradual dissection attempting to come down to the foreign body. The lips of the sclera are held aside by silk sutures (according to Mendoza's method). The foreign particle may appear in the uvea herniating into the incision if localization and dissection is accurate. Transillumination (with Lancaster's or Lange's instrument) applied to the opposite side of the globe is helpful. To avoid hemorrhage epinephrine 1:100 is dropped onto the scleral incision with thrombin solution to aid clotting. If the foreign particle lies a little deeper, then the ciliary body is incised radially. The particle is seized with forceps when it comes into view. If one waits a minute or two, it will at times present itself in the wound and can be removed. Prolapse of ciliary body is excised and the aforementioned Mendoza suture is tied closing the incision. The conjunctiva is closed with running suture. The same technique is followed for particles in the chorioid except that the site of incision in the sclera is surrounded with 6 surface coagulations. If the particle is magnetic and near the pars plana of the ciliary body, one can use the technique suggested by Verhoeff in 1932 and by Barbour and Fralick in 1941.

FOREIGN BODIES IN THE VITREOUS CHAMBER

For many years, eyes harboring copper or its alloys in the vitreous were given up to enucleation. Now newer techniques and instruments can save some of these cases. Several methods can be used. The choice of method depends on the location of the particle, on its visibility with the ophthalmoscope and on the cloudiness or bloodiness of the vitreous.

Method 1 for vitreous. Direct vision or *ophthalmoscope.* In a case with clear lens in vitreous and foreign body visible with ophthalmoscope without undue rotation of the eyeball. The sclera near the foreign body is bared. The site of incision is marked with gentian violet and surrounded by 6 to 8 surface coagulations. A 4 to 8 millimeter long incision is made in the sclera in the shape of capital I or T (with the

long arm of the letter meridional). The length of the incision is governed by the size and shape of the fragment. The uvea is exposed while the sclera is held aside with one or two Mendoza sutures. The uvea is incised with the cutting current of the diathermy. The particle may be seen glistening in the incision and is extracted with forceps and the sclera immediately closed with the above mentioned sutures. If the particle is not readily seen in the incision, one views it with the ophthalmoscope and extracts it with the author's self-closing vitreous chamber (23–24) forceps, introduced into the incision. The wound is closed as above. It may be touched with trichloracetic acid or 95 per cent phenol (18). The conjunctival incision is then sutured.

Vitreous: Method 2. Ophthalmic endoscope. The ophthalmic endoscope was devised in 1934 (25) and demonstrated that Spring in non-luminous form at the Section of Ophthalmology of the American Medical Association. In the Fall of 1934 (26), the self luminous model was demonstrated at the Academy of Ophthalmology and Otolaryngology. I have used it successfully in 5 cases. It has been used with success by Spaeth and others.

The endoscope consists of (1) a light carrier with a miniature lamp, (2) a special inverted Galilean telescope 2.5 millimeters in diameter, and (3) a small tubular forceps. These are held together in one plane by a metal sheath. There is an adjustable sleeve which can be preset for depth of entry of the forceps into the vitreous. The operative end of the instrument has a stop to prevent its being thrust into the vitreous chamber bodily. There is an electric connection which supplies current for the miniature lamp from a battery. The cross section of the operating end is 2.5 by 6.5 millimeters. The telescope affords a field of view 60 degrees in diameter. Thus at 10 millimeters' distance the field is 10 millimeters in diameter, at 15 millimeters' distance it is 15 millimeters in diameter. Thus, two thirds or more of the interior can be covered by moderate tilting of the instrument shaft. Particles at 15 millimeters' distance from the telescope end are magnified two diameters and become larger as they near the telescope. The inverted Galilean system permits everything to be in

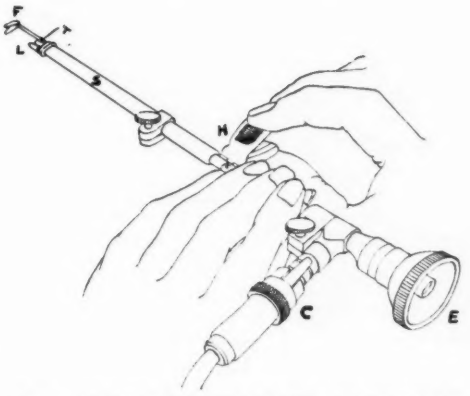

Fig. 17. Method of holding ophthalmic endoscope during operation. Surgeon's left hand holds and steadies the instrument body. The right thumb and index finger actuate the grasping forceps, *H*, whose blades, *F*, are seen just beyond the telescope, *T*, and miniature lamp, *L*, *S*, Adjustable sheath, *C*, electric battery connection, *E*, eyepiece.

focus except that the objects appear smaller as the distance from the telescope lens increases. This instrument should be used only in clear vitreous. The forceps used are shaped so that some may grasp a shot, while another is used for an irregular shaped splinter. They are either self-closing or manual closing.

It is of extreme importance for the surgeon who proposes to use this instrument to become thoroughly familiar with its application by working in a small light proof pill box (1 inch in diameter—about the size of the globe). The surgeon must learn to overcome the handicap of working with a monocular instrument. He must learn to hold it and handle it properly. He must learn to orient himself with the instrument at all times. After mastering removal of small objects from the pill box, one advances to practice with pig's eyes.

STERILIZATION OF OPHTHALMIC ENDOSCOPE

The instrument is washed with green soap, rinsed in distilled water, and sterilized by immersion for 20 minutes in 0.1 per cent mercury oxycyanide solution or 0.03 per cent mercuric phenyl nitrate. It is rinsed in sterile water and wiped dry. Alcohol, or heat sterilization or various chemicals, except the ones advised, will damage the lens cement and the fine electric insulation and will ruin the instrument.

When proposing to use the endoscope one begins with an accurate x-ray localization and a definite plan of operation. The approach may be between any of the recti muscles or beneath the superior or inferior rectus after they have been cut at their insertion to the globe. The lateral and medial rectus regions are avoided to prevent injury to the long ciliary arteries. The selected site for scleral incision is plotted with gentian violet and surrounded by surface diathermy coagulations or partly penetrating applications of the Kronfeld diathermy needle. This measure is for the prevention of retinal detachment. The incision is made 7 millimeters long in the meridional direction just down to the chorioid. Scleral sutures are inserted in the incisional margins to hold them apart and the ends of the incision are cut at right angles for 1 millimeter on each side and on both ends (so that the incision appears I shaped). Epinephrine 1 per cent solution and thrombin are applied to the chorioid surface and after 30 seconds wait the chorioid and retina are incised with diathermy or with scissors or with a shallow thrust of a cataract knife. The lips of the wound are held apart with sutures by the assistant and the endoscope is inserted just to the opening with the closed miniature forceps about 5 millimeters in front of the telescope and slightly to one side. The surgeon looks through the eyepiece of the illuminated instrument which is connected to an electric battery with preset rheostat. The assistant watches to see that the body of the instrument is not shoved or pushed into the globe. The surgeon sights the foreign body and grasps it with the forceps. The forceps is closed and pulled up to the telescope slowly and the entire instrument is withdrawn. During the procedure one assistant keeps the wound flaps against the sheath of the endoscope with his sutures so as to avoid loss of vitreous. On removal of the instrument he closes the incision and ties the scleral sutures. The conjunctiva is closed with running suture. Of 5 patients operated upon, one has 20/30 vision, another has 20/100 vision, a third case can count fingers. The fourth patient has a blind soft eye. The fifth case done in October 1946 has 10/100 vision with a partial traumatic cataract. This is a major procedure and the surgeon who uses this instrument should play with it for several weeks before he inserts it into an eye.

Vitreous: Method 3. Transillumination. By this method one exposes the sclera as above for transscleral approach. One or two small transilluminators are placed on the opposite side of the globe to the incision, thus illuminating the vitreous. The foreign body is outlined against the illuminated interior between the lips of the scleral incision. The foreign body is visualized and grasped with small serrated forceps. The incision is closed as in the first two methods. The sclera is also diathermized about the incision to seal off the retinal hole and prevent detachment. I have used this method in 3 instances and am favorably impressed by it. Schutz and Lindner have applied this method.

Vitreous: Method 4. Biplane fluoroscope. Cross has found the biplane fluoroscope useful in the removal of shot from the eye. Smaller objects do not cast sufficient shadow to be visible with the fluoroscope. He inserts a cross action wire forceps into the vitreous and is guided in his movements by the fluoroscopist. In the hands of Cross with the aid of his expert fluoroscopist, the method has proved successful in several cases. I have had no personal experience with this technique because of lack of a biplane fluoroscope.

Optic nerve. Foreign bodies in the head of the optic nerve can probably be removed with the ophthalmic endoscope. The damage to the nerve head with subsequent cicatrization would probably result in a blind eye. Although, removal of magnetic fragments from the nerve head is sometimes followed by moderately useful vision.

Nonmagnetic scleral foreign bodies. Scleral foreign bodies generally do little damage unless they project from either side of the sclera. They can be readily localized and dissected out and sometimes pried loose. If one is in doubt about the location of the foreign body, the sclera can readily be palpated with a probe or the end of a muscle hook. The site of the hard particle can be definitely felt.

Orbital foreign bodies can usually be left alone unless because of location or size they make pressure on vital structures or cause dis-

comfort and pain. They do not come within the scope of this paper.

Postoperative treatment. The postoperative management consists of:

1. *Antibiotics. Sulfadiazine* has proved the most successful agent in my experience for controlling infection. In fresh injuries, 30 grains is given on admission and is followed by 15 grains every 4 hours for 1 or 2 days. The dosage is then reduced to 15 grains every 6 hours for another 48 hours. Thereafter 15 grains are given 3 times daily for 3 to 4 days. Sodium bicarbonate in the amount of 10 grains is given with each dose and a liter of water is consumed daily. The urine is watched for crystals. The blood level of sulfadiazine is kept between 8 and 10 milligrams. The blood count is also watched for reduction in red and white blood cells and their differentiation.

Penicillin may be given intramuscularly. The first dose is 100,000 units in 5 cubic centimeters of ¼ per cent novocain. Thereafter, 25 to 50 thousand units are given intramuscularly every 3 hours for 3 to 4 days.

2. *Foreign protein therapy*—Tetanus antitoxin is given subcutaneously as a specific for the prevention of lockjaw in fresh injuries. Boiled milk in 10 cubic centimeters' amount for men and 8 cubic centimeters' dose for women and appropriate smaller dosage for children is given intramuscularly on admission to fresh injuries and every third day for 3 doses if indicated.

Typhoid A antigen is given intravenously instead of the intramuscular milk. The first dose is 15 to 20 million. It is increased by 15 to 20 million every third or fourth day as necessary. A reaction is desirable. Old people do not tolerate this therapy well.

3. *Atropine* is used postoperatively unless contraindicated by a rise in tension. Its application is delayed for 3 days in anterior chamber cases. (It is not used preoperatively in anterior chamber cases.)

4. *Daily dressings* are done for traumatic cataract and postoperative iritis for atropine instillation. Other intraocular cases are dressed every other day. Both eyes are usually kept closed for 1 week. Cases of retinal detachment or threatened detachment have both eyes kept closed for 2 to 4 weeks.

5. *Position in bed.* Patients with wounds of the cornea are required to lie flat in bed for 48 hours. Scleral wounds or incisions do best when kept flat for one week. Incisions in the lower sclera require several days longer in a flat position.

6. *Diet.* Liquid diet is given for 48 hours. Soft diet follows for 4 days. Light general diet is given after 6 days postoperatively.

7. *Bowels.* The intestinal tract is kept cleared by mineral oil given for 3 days. Simple enemas are given after 48 hours if necessary.

8. *Sedatives.* Codein sulfate in doses of ¼ to 1 grain may be given and repeated. Phenobarbital in ¼ grain doses is at times used as a sedative.

GENERAL RULES IN NONMAGNETIC INTRAOCULAR FOREIGN BODY CASES

1. Make a careful examination and take a complete history. Use every modern device for arriving at a complete diagnosis.

2. Get an idea as to the extent of trauma to the various structures and as to the impairment of function.

3. Assay the probability and extent of infection. Consider each case as potentially infected. Take prophylactic and therapeutic measures for its control.

4. Make an x-ray examination in each case with varied types of exposure and position. Stereoscopic x-ray films are valuable. Accuracy in localization is paramount.

5. Avoid removal of chemically inert foreign bodies unless they do harm because of size or mechanical irritation.

6. Avoid mutilating surgery and avoid groping in the vitreous. They lead to destruction of vision and of the globe.

7. Suspect and treat immediately all retinal detachments. Take precautionary preventive measures as outlined above.

8. Remove intraocular foreign bodies promptly to prevent their becoming enmeshed in exudate and organized scar tissue and also to prevent the damage that results from prolonged stay in the eyeball.

9. Multiple intraocular foreign bodies make conservative therapy a consideration of the first importance.

10. Do not overlook foci of infection and other systemic conditions that may delay healing and cause complications.

11. Have a definite well considered plan for each operation.

12. Know your surgical instruments thoroughly and be sure that they are in first class working order.

13. Be sure of the ophthalmic endoscope before attempting its use. This can only be had after continued and repeated practice so that its operation is automatic. When properly used this instrument may be invaluable in salvaging a potentially lost eye due to a retained nonmagnetic foreign body.

14. Scleral and corneal incisions and wounds heal faster and better when properly approximated by sutures.

15. The topical application of epinephrine 1:100 and thromboplastin or thrombin will often prevent destructive hemorrhage.

16. Enucleation is sanctioned only when the globe is collapsed and extensive vitreous loss has taken place and light perception is lost. Do not rush to enucleate when both eyes are injured.

17. Remember the danger of sympathetic ophthalmia. Three weeks is the safe period at the longest to temporize from the time of injury. A decision should be arrived at within 14 to 16 days as to enucleation of a potentially dangerous eye.

The subject was considered from the standpoint of adequate thorough survey of the injured patient including history and every necessary examination to arrive at an accurate diagnosis. Consideration was given to conservative treatment for chemically inert foreign bodies. Techniques were outlined for these measures and for simple accurate methods of x-ray localization. Operative techniques were described for the removal of nonmagnetic intraocular foreign bodies, from cornea, anterior chamber, iris, lens, ciliary body, vitreous, chorioid and sclera.

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VISUAL FIELD DEFECTS DUE TO HEAD INJURIES

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THE visual pathways are so extensive that injury to any part of the cranium may result, directly or indirectly, in defects in the field of vision. These pathways extend from the ganglion cells of the retina by way of the optic nerves, the chiasm, the optic tracts, the lateral geniculate bodies, and the optic radiations to the visual cortex in the occipital lobes. The additional cortex and fibers necessary for voluntary and reflex movements, visuopsychic functions, and association of one area with various other areas comprise a still more complicated and extensive network which involves every portion of the brain.

This paper will consider only the representation of various parts of the retina in the visuosensory cortex of the occipital lobes of the brain. An attempt will be made to summarize our present knowledge and to point out the difficulties in studying this subject. Proof that a given area of the cortex subserves a certain function is difficult as one seldom sees a clean-cut, isolated lesion to correlate with one's clinical findings.

First let us review the anatomy of the visual pathways. The nerve fibers from the temporal halves of each retina pass backward in the temporal portion of the optic nerve; they do not cross in the optic chiasm. Fibers from the nasal halves of the retina pass backward in the nasal portion of the optic nerve, but decussate at the chiasm. Fibers from the fixation area, or macula, form the papillomacular bundle which enters inferotemporally and then assumes a more central position. In the chiasm these fibers lie posteriorly and undergo semidecussation.

Behind the chiasm are the optic tracts, each of which is made up of (1) fibers from the temporal portion of the retina of the same side, (2) fibers from the nasal half of the retina of the opposite side, and (3) macular fibers from the temporal half of the same side and from the nasal half of the opposite side. Thus the macular fibers may be said to form a minor chiasm within the major chiasm. This semidecussation of the central fibers is most important, as we shall note again.

The least possible confusion will be had if we look upon the central area of the field as having the same characteristics as the peripheral field. The optic tracts remain condensed throughout their course and end in the lateral geniculate bodies.

From the geniculate bodies to the occipital cortex we find the optic radiations. The geniculocalcarine fibers lie in the internal capsule behind the sensory fibers and internal to the auditory fibers. Fibers from the upper retinal quadrants (lower portion of the visual fields) lie dorsally, while fibers from the lower retinal quadrants (upper fields) lie ventrally. In the anatomical space between these lie the macular fibers (the central field). Some of the ventral fibers detour into the uncinate region of the temporal lobe around and over the anterior horn of the lateral ventricle before bending backward along the lower aspect of the ventricle to end in the anterior portion of the lower calcarine cortex. These fibers correspond to the temporal crescents of the field. The majority of the fibers in the optic radiations pass directly to the calcarine cortex.

Observers have diverse opinions regarding the representation of the fixation area, or macula, in the cerebral cortex. A review of their reasons would serve no useful purpose here.

The visual cortex occupies part of the medial surface of each occipital lobe and posteriorly the visual area extends a little onto the lateral surfaces. The visual area extends from the tip of each lobe, where the fixation area is represented, forward to the splenium of the corpus callosum at the anterior end of the calcarine fissure where the periphery of the retina is represented. The lingual gyrus lies below and the cuneus above the calcarine fissure. The upper portion of each retina is represented in the area above the calcarine fissure,

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while the lower portions of the retinas are represented below the calcarine fissure. Sectors adjacent to the vertical meridian of the retina are represented along the lips of this fissure, while sectors to the sides of the horizontal meridians are projected in the depths of the fissure. The temporal crescents of the binocular fields are represented in the oral parts of the calcarine fissure.

The cortical area representing the fixation area is quite extensive as compared with the area representing the peripheral portions of the visual fields. This is analogous to the large motor and sensory areas in the parietal cortex representing finger and thumb as compared with the area representing trunk.

It is unfortunate that our methods of studying cerebral localization are so limited. Obviously we cannot induce lesions in human subjects, nor can we obtain subjective responses from animals. Electrical stimulation of the visual cortex of man results in responses less precise and more difficult to interpret than the responses invoked by test objects used in taking visual fields. Electroencephalography has so far shown little promise as a method of studying the visual apparatus. Complete neurological and ophthalmological examinations are our best methods, and plotting of the visual fields the most satisfactory single test.

Four types of lesions in the brain can be correlated with visual field defects. Each of these has its disadvantages and limitations. Vascular lesions have provided valuable information regarding cerebral localization. However, individual variations in blood supply are not infrequent. Occlusion of certain cerebral arteries is common, but occlusion of smaller branches supplying small areas of the cortex is not common.

While some tumors produce clean-cut field defects, much depends upon the time of study of an expanding lesion. Infiltrating tumors have indefinite borders. Local or distantly applied pressure from a tumor may result in atrophy, edema, or vascular occlusion in areas remote from the space-taking lesion.

Excision of tumors or of scar tissue allows the neurosurgeon to note the exact area involved. This is our best method of clinical study.

Injuries provide the next best method. One must keep in mind several factors which may affect the interpretation of traumatic lesions. One of these is the element of time as hemorrhage, edema, and contusion produce varying pictures.

Regardless of the lesion studied, postmortem examination with sections of the entire brain is by all odds the most reliable.

Among the factors that render interpretation of visual field defects due to injuries hazardous or difficult are these:

1. Depressed skull fractures produce effects which are at least partially reversible by elevation of the fragments.

2. Foreign bodies may be found at one site, but have traversed important structures in reaching this site. It is therefore most important to know the location of the entire tract of a foreign body.

3. Blood vessels may be torn or thrombosed, giving the picture of a vascular lesion alone or a combination of vascular, cortical, and radiation fiber injury. Indeed, vascular injury may play a rôle in a high percentage of field defects due to trauma. We may say that it is unimportant to know whether damage to cortical cells is direct or due to loss of blood supply. However, the field defect is likely to be larger in a vascular injury. The prognosis is often much better when the blood vessels are only partially or temporarily occluded. It is important to remember that terminal branches of the calcarine and middle cerebral arteries do have anastomoses in the pia before piercing the cortex.

4. Edema from any cause may be responsible for transient effects on the visual fields.

5. A brain abscess may be a late, unsuspected complication of injury and add its effects to the visual field defect.

6. The neurosurgeon may not be able to tell how much of the lesion is destructive and how much is due to edema, hemorrhage, or contusion. He is handicapped in observing landmarks and often cannot see the entire extent of the injury because of the small opening in the calvarium through which he operates. The brilliant work of the neurosurgeons in the past war has kept alive many men who would otherwise not have returned to us for examina-

tion. We would like to have had more complete neurosurgical notes, but we also understand why they are not available.

When the ophthalmologist is plotting and interpreting visual fields, it is essential that he bear in mind the fact that injuries other than the one producing the field defect may affect the results obtained. Listing of some of these factors may help to illustrate this point:

1. The patient may not understand what is expected of him during the test.

2. Emotional instability and fatigue may affect the result. It is not easy for even a normal person to have his fields checked.

3. Hysteria and malingering may be responsible for part of the defect. One usually thinks of hysteria and malingering as "pure" or isolated phenomena. A patient who has sustained a genuine injury resulting in partial loss of his visual field may exaggerate this loss of his field because of fear or a desire to obtain a greater disability pension.

4. Paralysis of extraocular muscles may result in apparently defective visual acuity or defects in the visual field which disappear when the head is placed in the proper position. Paralysis of the sixth nerve or conjugate deviation of the eyes are two examples. Here again there may be a true field defect exaggerated by improper position of the patient.

5. Poor response due to involvement of Wernicke's auditory area (areas 41 and 42 of Brodman) may prevent proper responses to vocal instructions.

6. Involvement of the motor speech area of Broca (area 44 of Brodman) may result in poor vocal responses from the patient.

7. The patient may have difficulty in fixing or maintaining fixation of the target because of poor visual acuity, central scotoma, or a hemianopic defect with splitting of the fixation area. Conversely, patient may seem to maintain fixation better than he actually does.

8. The visuopsychic areas may also be involved and make it difficult or impossible for the patient to give adequate responses when being tested.

Area 18, the parastriate area, surrounds the visuosensory area (17) in the occipital cortex. A lesion here prevents a patient from recognizing an object even though he sees it.

Area 19, the peristriate area, surrounds area 18. The patient may see (area 17) and recognize (area 18) but be unable to remember or revisualize the characteristics of an object.

Because of the proximity of areas 17, 18, and 19 more than one area may be destroyed by the injury.

9. Lesions in the parietal lobe:

Area 39, lying anterior to area 19, in the angular gyrus of the parietal lobe has to do with interpretation of symbols, combining recognition and revisualization (which are dealt with separately in areas 18 and 19).

Area 40 deals with mathematical figures and calculations. It is located in the supramarginal gyrus of the parietal lobes.

Areas 39 and 40 are said to be more dominant than areas 18 and 19.

10. Disturbances of higher psychic and association areas may also interfere with proper testing of the visual fields.

Some of the factors listed above are of practical importance and easily demonstrated. Those which deal with psychic and association functions are listed as of theoretical interest as our precise knowledge is too limited for practical clinical application. The opportunity for further study is with us today as never before because of the many service men who have survived a great variety of head injuries. It is to be hoped that Veterans Hospital staffs will follow these patients carefully with repeated neurological, neurosurgical, ophthalmological, and finally with postmortem studies. When the injured brain is fixed and studied grossly and microscopically, we can find the true extent of the lesions which resulted in visual field changes observed during life. This should settle many disputed points—but will do so only if our clinical notes are accurate and complete.

If this demonstration stimulates others by its inadequacies rather than by its excellence of detail, its purpose will have been served.

CASE REPORTS

These cases were collected in conjunction with Dr. J. N. Greear, Jr. now in Washington, D.C., and formerly Chief of Eye Section, Valley Forge General Hospital.

CASE 1. This patient sustained a fracture of the left parietal and occipital bones with multiple depressed fragments of bone, laceration of the dura and

brain, and an intracerebral clot. Craniotomy was performed 2 days later, followed by drainage of cerebrospinal fluid for a period of 4 weeks.

Roentgenogram of the skull showed an oval area of bony dehiscence measuring 5 by 3 centimeters in the posterior portion of the left parietal bone and anterior portion of the left leaf of the occipital bone.

The field defect was right homonymous hemianopsia with sparing of the fixation area and a portion of the right field adjacent to the vertical meridian. Visual acuity was 20/15 J1 in each eye.

The site of injury, data obtained at operation, plus the field defect indicate a lesion of the left occipital cortex, probably vascular in type. Sparing of fixation is due to the dual blood supply to the cortex.

CASE 2. This patient sustained a severe compound, comminuted fracture of both leaves of the occipital bone, with stellate fractures of both parietal bones. Multiple foreign bodies were seen at a depth of 5 to 6 centimeters in the left parieto-occipital area.

Craniotomy was performed the next day. Débridement left a 6 by 3 centimeter defect in the occipital bone. A hematoma and damaged tissue of the brain were removed; the foreign bodies were not removed from the left occipital lobe.

The patient was apparently blind for a period of 15 days, during which time both pupils reacted to light. He also showed sensory aphasia and generalized hyperreflexia. Bilateral papilledema was present for a considerable length of time before subsiding spontaneously.

Roentgenogram showed a 4 by 8 centimeter defect in the occipital bone, more to the left side. Linear fractures radiated in all directions from this defect. Two large foreign bodies were present in the parietal lobe 9 centimeters above the mastoid bone.

The field defect was right homonymous hemianopsia with division or splitting of the fixation area. Visual acuity was right eye, 20/70 plus 2 J12 and left eye 20/100 plus 1 J12. Degenerative changes visible in the nerve heads and maculas, a result of prolonged papilledema account for the decreased acuity.

The information obtained at operation plus the field defect place this lesion in the left occipital cortex and deeper tissues of the brain. The sensory aphasia and hyperreflexia were due to damage to the parietal lobe.

CASE 3. This patient sustained a penetrating wound of the skull and both occipital lobes by a shell fragment which entered the left occipital and came to rest in the right occipital lobe. The foreign body was removed and débridement carried out.

X-ray examination showed a large surgical defect involving the inion and upper portion of the occipital bone—with fracture lines radiating into the left parietal bone and to both petrous pyramids.

Visual acuity was right eye ability to count fingers at 1 foot nasally and left eye at 3 feet temporally. There was conjugate deviation of the eyes to the right; pupils reacted to light; fundi were normal.

The field defect was right homonymous hemianopsia plus a small central defect in each field. Damage to the entire left visual cortex and to the tip of the right occipital lobe by the foreign body accounts for the field defect.

CASE 4. This patient was struck by mortar shell fragments, sustaining a compound, comminuted fracture of the occipital bone with depressed fragments driven into right occipital lobe of brain.

Two days after injury craniotomy was done. The tip of the right occipital pole and the calcarine area were destroyed by the fragment of bone. The dura was torn on both sides of the midline. The longitudinal sinus was thrombosed. The patient was unconscious for 11 days. Examination on about the fourteenth day showed complete blindness lasting several more days. Later the patient showed homonymous hemianopsia by the confrontation method. The fundi were normal. Vision was reduced to ability to count fingers.

X-ray examination showed a 4.5 by 6 centimeter defect in the middle of the occipital bone with a stellate fracture extending into the right parietal bone.

The last field examination showed a left homonymous hemianopsia plus loss of part of the right lower quadrants of the field and involvement of both fixation areas. The field defect is explained by damage to the right calcarine area and tip of the right occipital lobe. The left occipital lobe must have been damaged above the calcarine fissure with injury to the tip of the occipital lobe or the central fibers beneath the cortex.

CASE 5. This patient was injured in a plane crash, sustaining a compound, depressed skull fracture in the midoccipital region. Thirty-six hours later the depressed fracture was elevated. Two fragments just to the right of the midline were found 1.5 centimeters below the dura piercing the longitudinal sinus. A larger portion of the right leaf was pried outward into proper position. The dura was intact except at the longitudinal sinus. The field defect 4 weeks later was a left homonymous hemianopsia sparing the fixation area. Vision was 20/30 J1 in each eye.

Four months later the field defect was a left homonymous lower quadrantopsia with sparing of the fixation area. Vision had improved to right eye, 20/15 J 1 and left eye 20/20 J 1.

Here we know that the right occipital cortex was damaged. The improved fields are explained by recovery from edema or contusion of the cortex adjacent to the destroyed cortex.

CASE 6. This is one of two patients with bilateral homonymous hemianopsia with sparing of the fixation area and retention of good central vision in each eye. This patient was injured by artillery shell fragments, sustaining a compound, depressed fracture of the left leaf of the occipital bone and several foreign bodies in the left frontal lobe of the brain.

On the day of injury the wound was débrided and the longitudinal sinus packed with muscle tissue to arrest bleeding. One week later the patient was completely blind, had a bilateral papilledema, but his pupils reacted to light.

On the eighth day after injury a second craniotomy was done, evacuating a subdural hematoma which was compressing the left occipital lobe by 1.5 centimeters. When the necrotic tissue of the brain was removed, a defect 3 centimeters deep remained. Then a clot was removed from the right occipital lobe whose cortex was largely liquefied. The neurosurgeon's operative note states, "There was considerable damage to both occipital lobes, thus accounting for the blindness. The damage, however, did not appear to me to destroy the calcarine area completely, and it may be that after edema subsides, vision may return, particularly in the upper fields."

Three weeks after injury the patient had light perception. Vision gradually improved. Eight months later, vision was right eye, 20/40 J 6 and left eye 20/20 J 1.

Visual fields showed loss of all but the central one degree. The patient can read only one letter at a time, but he says he sees this clearly.

We have definite evidence of severe damage to both occipital lobes and a note that all of the calcarine area did not appear to be destroyed. There must be damage to the anterior portion of the calcarine areas, and undoubtedly to the optic radiations.

In these patients we must be on the lookout for hysteria or exaggeration of the field defect despite the genuine severe injury. That is, they must have a large field defect, due to injury, but for some reason may show too much loss. A medical officer once told me of suspecting a patient with such a field of getting around too well. Under sodium amytal the patient confessed that he had a wider field, but because of a personal problem he elected to show this limited field.

So far as we were able to ascertain 2 of our patients actually had this type of field. Similar cases have been described by Gordon Holmes and by Scarlett and Ingham after World War I. McDonald has described bilateral homonymous hemianopsia due to bilateral occlusion of the calcarine arteries. A vertical strip of field was retained below the spared fixation area.

CASE 7. This patient showed field defects which are the antithesis of the last one. That is, he has bilateral central scotomas with normal peripheral fields.

He was injured by shrapnel, sustaining a depressed fracture of the occipital bone with multiple foreign bodies. The next day débridement of the wound was carried out. Three days later vision began to improve and did so for 2 months. Four months after injury the depressed fracture was elevated, pieces of bone and shrapnel were removed from the right occipital lobe. Both occipital lobes were found contused and degenerated, some of the cortex being replaced by xanthochromic scar tissue.

Vision was 20/200 J 0, eccentric, in each eye.

The peripheral fields were normal. The central fields showed bilateral central scotomas, with most of the scotoma to the right of the midline. Injury to the cortex at the tip of both occipital lobes, especially the left, accounts for the field defect.

Gordon Holmes has shown a variety of homonymous central field defects, both unilateral and bilateral.

SUMMARY

A review of the anatomy of the visual pathways has been given.

The areas of the visual cortex representing all parts of the retina (or of the visual fields) have been pointed out.

An attempt has been made to show the difficulties encountered in studying the visual cortex.

Seven illustrative case reports are given.

It is hoped that Veterans Hospitals will compile extensive data on causalties of this type, following through to postmortem examination as this is the only reliable method of determining the many things we do not know about cerebral functions. The opportunity is greater than ever before, and, we trust, shall never be so great again.

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THE FENESTRATION OPERATION

An Evaluation of Its Present Status

GEORGE E. SHAMBAUGH, Jr., M.D., Chicago, Illinois

THE consensus of published reports indicates that the fenestration operation has taken its place as an accepted otologic procedure for certain cases of deafness due to otosclerosis. In evaluating the scope of usefulness of the operation at the present time there are 6 important questions that we should try to answer.

1. Which patients should be operated upon?
2. Which technique yields the best results?
3. How does the hearing after operation compare with a hearing aid?
4. Can the operation arrest or prevent the nerve degeneration of otosclerosis with stapes ankylosis?
5. What are the risks?
6. How permanent are the hearing improvements?

WHICH PATIENTS SHOULD BE OPERATED UPON

The first question of which patients should be operated upon has been discussed in the literature by a number of otologists, with general agreement except on one point. Otologists who have had experience with the fenestration operation agree that the external and middle ear should be free from any active or recent inflammation, that the eustachian tubes should be normally patent, and that the drum membrane should be intact. They also agree that the ideal patient for operation has a stapes fixation with normal cochlear function as evidenced by the masked bone conduction audiogram within normal limits for the speech frequencies, with an air conduction audiogram averaging 40 decibels or more loss for the speech frequencies (Fig. 1). The point of disagreement lies with those patients who cannot be classed as ideal because one or more of the speech frequencies by bone conduction is below the normal range. Should the operation be refused these patients, as some have advised, or should the otologist consent to operate if the patient clearly understands that he cannot expect to attain the 30 decibel practical level?

Last spring the American Society for the Hard of Hearing, through Dr. Fowler, mailed out to its members, who had had the fenestration operation, the following questionnaire (Fig. 2). To aid this evaluation of the operation from the patient's viewpoint, two copies of the questionnaire were sent to each of my patients operated upon since I began this work 8½ years ago, with the request that one copy be mailed to the American Society for the Hard of Hearing in Washington, and the second copy be mailed to the Chicago society. Through the gracious co-operation of the Chicago society, I have been able to study these replies.

Before presenting the results of this inquiry, let me make it perfectly clear that I am fully aware of the errors inherent in any such attempt to evaluate a medical procedure, for patients are notoriously prone to psychological reactions that may distort their judgment concerning the value and results of any therapy. Nevertheless, it would be a mistake to disregard entirely the patient's subjective evaluation of his operation, provided we also insist upon objective audiometric proof of a sustained hearing improvement.

A total of 853 patients operated upon by me were mailed the questionnaire, and 623 replies were received. These were divided into 5 groups:

Group I. Operation successful in all respects: hearing has remained improved; family regards operation warranted in view of the results; the patient does not now wear a hearing aid; *the patient would have the operation performed again were he to experience the same results.*

From the Northwestern University Medical School.
Presented before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16-20, 1946.

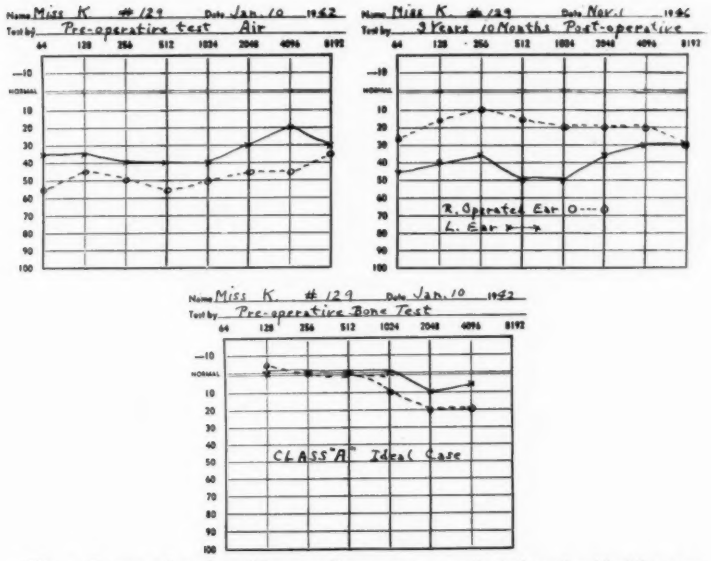
Name Miss K. # 129 Date Jan. 10 1942
Test by Pre-operative test Air
64 128 256 512 1024 2048 4096 8192
—10
NORMAL
10 20 30 40 50 60 70 80 90 100
Name Miss K. # 129 Date Nov. 1 1942
Test by 3 Years 10 Months Post-operative
R. Operated Ear o---o
L. Ear x---x
Name Miss K. # 129 Date Jan. 10 1942
Test by Pre-operative Bone Test
CLASS "A" Ideal Case

Fig. 1. Preoperative air and bone audiograms on a patient classed as ideal for operation, and postoperative air audiogram.

Group II. Operation successful in that family regards it warranted by the results and patient would have it performed again for the same results, *but* a hearing aid is still worn on certain occasions.

Group III. Family regards operation as not warranted by the results, but patient would have it performed again were he to experience the same results, and he does not now wear a hearing aid.

Group IV. Too soon after operation to be able to answer all of the questions.

Group V. Failure. Patient would not have the operation performed again were he to experience the same results.

Of the 623 replies, 516 or 82.8 per cent regard the operation as successful in all respects; 25 or 4 per cent regard it as successful, but still use a hearing aid at times; 7 or 1 per cent regard it as successful, but the family is doubtful; 8 or 1 per cent wish to wait a while longer before committing themselves; 66 or 10.6 per cent regard the results as a failure (Table I).

1. Name:
2. Date of fenestration operation:
3. By whom performed?
4. State of hearing immediately before and following the operation, audiogram if available:
5. State of hearing one year following operation, audiogram if available:
6. State of hearing at present time, audiogram if available:
7. Effect on hearing for conversation: (Better_____No change_____Worse_____.)
8. What is the opinion of your family in regard to the operation? In view of the results, was it warranted? Yes_____No_____.
9. Do you still use a hearing aid? Yes____No____.
10. Would you have the operation performed again if you were to experience the same results? Yes_____No_____.
11. Will you please add any other comments you believe might be helpful to others contemplating the operation.

Fig. 2. Questionnaire sent to patients who had had the fenestration operation.

TABLE I.—REPLIES TO QUESTIONNAIRE RECEIVED FROM PATIENTS WHO HAD HAD FENESTRATION OPERATION

	Replies	Percentage of total
Group I (Successful).....	516	82.8%
Group II (Partial Success)...	25	4%
Group III (Partial Success)..	7	1%
Group IV (Undecided).....	8	1%
Group V (Failure).....	66	10.6%

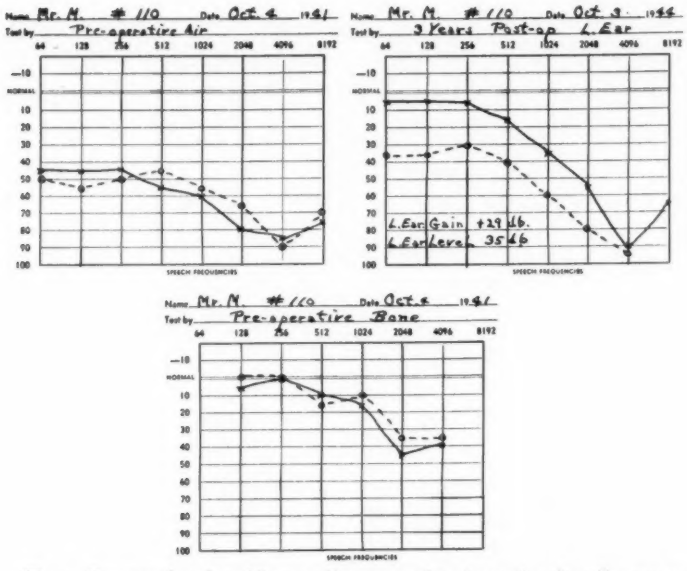
Mr. M. # 110 Oct. 4 1941
Pre-operative Air
Mr. M. # 110 Oct. 3 1946
3 Years Post-op L. Ear
L. Ear Gain +29 46.
L. Ear Level 35 46
Mr. M. # 110 Oct. 4 1941
Pre-operative Bone

Fig. 3. Preoperative air and bone audiograms and postoperative air audiogram on a patient who regards the operation as successful but whose hearing did not reach the 30 decibel practical level.

When we study the individual patients who regard the operation as successful in all respects (Group I) we find that 303 of the 516 reached the 30 decibel practical level as a result of the operation; 71 more were within 5 decibels of the practical level, while 142 have a loss of more than 35 decibels for the speech frequencies How can these patients regard the operation as successful? The answer is that many of them gained so much for the lower frequencies that they can compensate in part for their relatively poor hearing for the speech frequencies (Fig. 3). Others were so profoundly deafened before operation that the improvement has been of great practical value even though it failed to bring them to the 30 decibel level of practical hearing. In other words, the number of decibels that a patient gains is important to him, as well as the final hearing level that he attains.

The second group is also of interest. These patients regard the operation as successful, but they still use a hearing aid at times (Fig. 4). Here again we have patients with a profound preoperative loss, some of whom were unable to wear a hearing aid because of their profound loss, but who now obtain very good results with a hearing aid, and therefore regard the operation as worthwhile. Many of these patients state that the hearing results from the operation far exceeded their expectations.

From our experience and observation, we believe that the fenestration operation has 2 important fields of usefulness: first in patients with stapes fixation and normal hearing by bone conduction, where we have a good chance of restoring practical hearing, and second in patients who are profoundly deafened and show beginning nerve degeneration where we cannot expect to bring the hearing to the practical level, but where, with a definitely guarded prognosis, the patient will usually gain enough hearing to regard the operation as very much worthwhile.

The following classification of cases for operation is suggested:

Class A. Ideal: Normal hearing by bone for speech frequencies. Prognosis: 8 in 10 chances of a permanent hearing improvement within the 30 decibel practical level (Fig. 1).

Class B. Suitable, but not ideal: Normal hearing by bone except for one of the speech

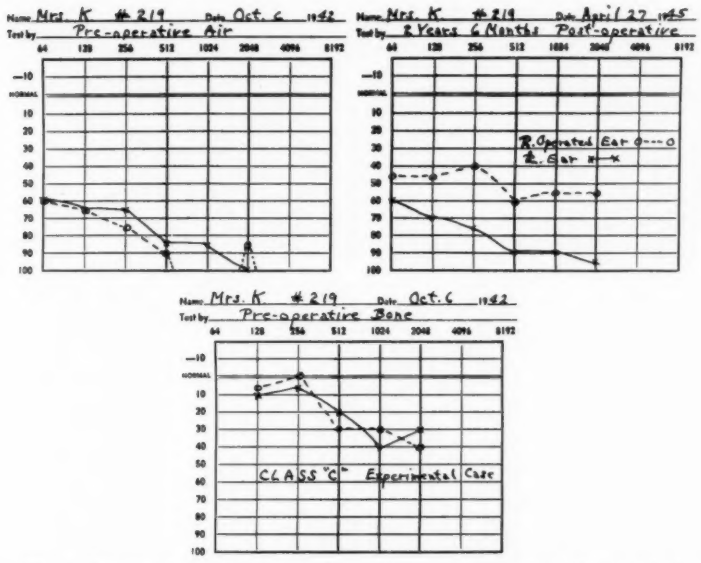
Name Mrs. K #219 Date Oct. 6 1942
Test by Pre-operative Air
64 128 256 512 1024 2048 4096 8192
NORMAL
Name Mrs. K #219 Date April 27 1945
Test by 2 Years 6 Months Post-operative
R. Operated Ear o---o
L. Ear x---x
Name Mrs. K #219 Date Oct. 6 1942
Test by Pre-operative Bone
CLASS "C" Experimental Case

Fig. 4. Preoperative and postoperative audiograms on a patient who regards the operation as successful because she can now wear a hearing aid with excellent results and before operation she could not use a hearing aid because of the profound hearing loss.

frequencies that shows a loss of 30 decibels or more. Prognosis: 50–50 chance of sufficient gain to do without a hearing aid (Fig. 5).

Class C. Experimental: Two or more of the speech frequencies show a 30 decibel or greater loss by bone, but the Rinne' test for the 1024 fork is negative. Prognosis: A remote 1 in 10 chance of sufficient improvement to give practical hearing without an aid (Fig. 6).

Class D. Unsuitable due to incomplete stapes fixation, or to profound nerve degeneration. Prognosis: Operation contraindicated.

In all cases in which there is a substantial difference to the patient in the useful hearing in the two ears the poorer hearing ear should be selected for operation. If the poorer hearing ear falls in class B, and the better ear in class A, the poorer ear should still be operated upon first, and if the operation is successful, making this the better ear, the second ear may then be operated. *As long as the fenestration operation has a chance of making the hearing in the ear operated upon permanently worse we are not justified in risking the patient's better hearing ear. If we cannot always improve the hearing by the fenestration operation, at least we shall not be destroying the patient's useful hearing.*

The bone conduction audiogram should always be made with adequate masking of the opposite ear.

In selecting cases for operation the tuning fork tests are a valuable adjunct to the air and bone audiograms. These four tuning fork tests are particularly helpful:

1. If the patient cannot hear the 64 fork at maximum intensity close to the ear, the stapes may be regarded as completely ankylosed. If the 64 fork is audible by air at moderate intensity the stapes fixation is only partial and the fenestration operation is not indicated because there is too little to be gained. Later in the disease, when the stapes is more completely fixed and the 64 fork is scarcely heard at maximum intensity, or is not heard at all by air, the operation may become indicated.

2. If the Rinne' test with the 1024 fork is negative, using masking of the opposite ear, the hearing should be improved by the operation, even though the patient is a B or C case.

3. If the Rinne' test with the 512 fork using masking is positive the stapes fixation is only slight and operation is contraindicated.

4. If the 2048 fork is not heard by bone using masking the prognosis is very poor and the patient should be considered a C or D case even with normal hearing by bone for the 512 and 1024 frequencies.

The otologist who is beginning this work will do well to confine his operations to class A cases. As his experience increases and his results improve he may consent to operate on class B cases, but only after the patient clearly understands the definitely limited prognosis. Class C cases are better not operated upon, and if possible should be persuaded to wear a hearing aid.

WHICH TECHNIQUE YIELDS BEST RESULTS

The second question that we should answer in evaluating the present status of the fenestration operation is: Which technique yields the best results? This question cannot be answered until accurate statistics are available on the results obtained by the various techniques that have and are being used. It is our belief that the future rapid advancement of the surgical treatment of otosclerosis depends more than anything else upon the complete and accurate reporting of results by all otologists who advocate a new technique. There is no other way by which we may judge the relative merits of different techniques and there is no other way to protect ourselves and our patients from the hasty adoption of a new, but inferior technique on the basis of vague, misleading, incomplete or hasty reports. So important to the future of this work is this question that I wish to devote part of this paper to a consideration of statistical studies as they apply to the fenestration operation.

A few years ago a group of otologists interested in the fenestration operation agreed to contribute their records for statistical analysis to compare the results obtained by different techniques. This co-operative undertaking soon proved unsuccessful because of the failure of some to contribute their records. I should like to propose that some larger organization with authority and prestige, such as the American Otological Society, or the American College of Surgeons undertake an impartial study and investigation of results obtained by different fenestration techniques.

The surgical treatment of otosclerosis lends itself ideally to a statistical analysis of results because we can measure these results objectively in terms of decibels. First, a uniform method of making audiometric tests and of keeping records should be recommended. Second, there should be an impartial periodic spotcheck of the records and audiometric tests of each otologist to insure sufficient uniformity and reliability of records, and statistics. Third, methods of statistical analysis and interpretation of results should be agreed upon; and, fourth, a periodic, perhaps annual, publication of the results obtained by different surgical techniques will permit an accurate and scientific evaluation of their relative merits.

To encourage such a program to further the improvement and development of the surgical treatment of otosclerosis along scientific lines, my associate, Dr. Juers, and I offer to provide every facility for an impartial study and analysis of our records and results on all of our patients operated upon since we began this work 8½ years ago. The system that we have used for keeping our records and for tabulating our results has proved satisfactory for our own purposes in comparing our own results as we have modified the operation from time to time. This system might be applicable to the larger study that we propose.

To minimize the apparent hearing improvement between the first audiometric test and subsequent tests due to the patient learning how to respond to this examination the preoperative hearing level is determined by 3 preoperative tests made on different days, except in rare cases in which patients come from distant places and only 2 preoperative tests may be secured. The threshold of hearing for 512, 1024, and 2048 cycles from the three preoperative audiograms is averaged as the preoperative hearing loss for the speech frequencies. After operation the patient's hearing is tested at approximately 2, 4, and 6 weeks, and 3 months, 6 months, and 1 year after operation, and at least once a year thereafter for the rest of that patient's life. When the patient has come from afar, it may be impossible to re-

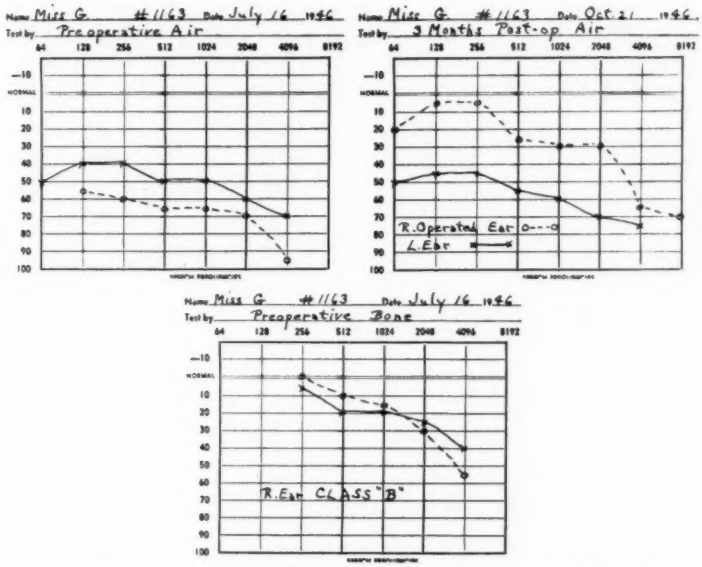
Name Miss G. #1163 Date July 16 1946
Test by Preoperative Air
64 128 256 512 1024 2048 4096 8192
NORMAL
Name Miss G. #1163 Date Oct. 21 1946
Test by 3 Months Post-op Air
R. Operated Ear o---o
L. Ear
Name Miss G. #1163 Date July 16 1946
Test by Preoperative Bone
R. Ear CLASS "B"

Fig. 5. Preoperative and postoperative audiograms on a patient classed as suitable but not ideal for the fenestration operation.

turn for all of these followup audiograms, in which case we must rely upon tests made elsewhere. We use this record card (Table II) for recording repeated audiometric tests and the improvement or loss following operation in the ear operated upon and not operated upon.

Our audiometer is calibrated so the normal hearing individual will give a threshold reading within 5 decibels of the 0-line in our soundproof rooms. We use the interrupted tone technique and take the first intensity that the patient consistently hears coming from inaudibility to audibility as the threshold. These minutiae of testing technique are important, for by using a continuous tone, or by testing from audibility to inaudibility, a threshold reading will be obtained 5 or 10 decibels higher than by the technique that we employ. Such a difference in methods of testing could lead to false conclusions concerning the relative merits of 2 surgical techniques, if the success of the operation be measured solely by the decibel level achieved by the patient. Since the technique of audiometric testing is not standardized, we believe that a second method of judging results should also be employed, namely, a consideration of the number of decibels of hearing gained by the operation. This method has the further advantage that it automatically compensates for the differences in the preoperative hearing level of patients chosen for surgery by different operators. Thus, a surgeon who selects patients with an average preoperative loss of 45 decibels will obtain a higher percentage of cases that reach the 30 decibel practical level as compared to another surgeon whose patients have an average preoperative loss of 55 decibels. If we measure the results solely by the hearing level attained we could be misled in appraising the relative merits of two different techniques. Therefore, we advocate that the results of surgery be measured both by the number of decibels gained, and by the final hearing level attained.

To make our results readily accessible for statistical study by ourselves and by others, we keep the essential data on every patient operated upon summarized on a "fenestration score board." This consists of a visible index system on which are recorded each patient's serial number, name, date of operation, the highest hearing improvement in terms of deci-

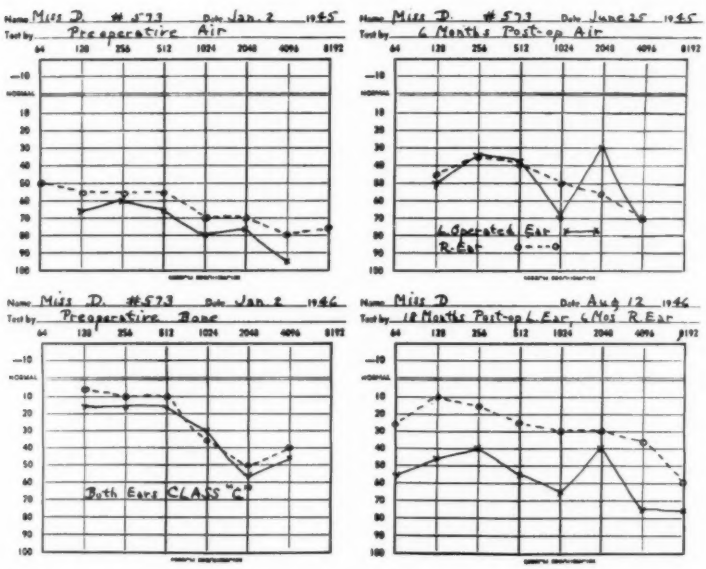

Fig. 6. Preoperative and postoperative audiograms on a patient classed as an experimental candidate for the fenestration operation.

bels gained for the speech frequencies with the time after operation of this test, and the most recent hearing result with the decibels gained or lost for the speech frequencies, the time after operation of this test, and the final hearing level. Every time a patient returns for an audiogram the strip with the above data is replaced with a new strip incorporating his latest test. To facilitate a statistical calculation of results colored indicators are used as follows:

Orange: Hearing worse (loss of more than 10 decibels for speech frequencies).

Yellow: Hearing unchanged (within 10 decibels of preoperative level).

Green: Hearing improved; but improvement subsequently lost.

White: Hearing gain of 10 to 30 decibels for speech frequencies.

Blue: Greater than average gain of 30 to 40 decibels.

Purple: Exceptionally great hearing improvement of more than 40 decibels for the speech frequencies.

Pink: Hearing within the 30 decibel level.

Red: Hearing within the 20 decibel level.

By means of these colored indicators one may find at a glance the percentage of good and bad results in the 90 cases tabulated on each board. A change of 1 decibel in a patient's audiogram may shift the result from one classification to another, and since repeated audiometric tests always show a fluctuation of a few decibels any statistical calculation will fluctuate slightly from month to month. The general average, however, remains approximately constant with a given technique.

Until statistical material such as I have described becomes available on all techniques, we cannot answer the important question of which one gives the best results. We can only present our own data and hope that others do likewise. We invite any of you to check our records, our scoreboards, and to examine our cases at any time.

The technique which we are using at Northwestern University Medical School has been described recently in the literature. Briefly, it makes use of the Lempert nov-ovalis fenestration operation with the addition of certain features to inhibit osteogenesis. These are:

TABLE II.—AUDIOMETRIC RECORD CARD FOR PATIENTS WHO HAVE THE FENESTRATION OPERATION.

Name Mrs CVM									Right ear		Date 2/22/40 Age 31								Left ear	
Date	64	128	256	512	1024	2048	4096	8192	Average for speech	Change for speech	64	128	256	512	1024	2048	4096	8192	Average for speech	Change for speech
2/22/40	50	45	50	55	60	50	65	75	55		40	35	40	50	50	50	65	75	50	
2/29/40	55	50	55	60	70	45	70	80	58		40	35	45	50	50	50	65	75	50	
3/7/40	50	40	50	60	60	50	65	70	57		35	30	45	55	50	50	65	75	50	
3/13/40	Fenes	tratio	n Rea	r (La	st 3x)				(57)										(50)	
3/26/40	35	30	40	45	35	15	70	75	32	+25	40	30	45	50	50	45	80	75	48	+2
4/8/40	30	25	35	45	35	10	65		30	+27	40	30	40	50	50	45	65		48	+2
4/16/40	30	25	35	45	35	15	70		32	+25	40	35	45	50	50	50	70	75	50	0
4/29/40	40	35	40	45	50	15	70		37	+20	40	30	40	50	50	50	70	75	50	0
5/6/40	30	30	30	40	40	10	60		30	+27	35	35	40	50	50	45	60	75	48	+2
5/16/40	35	30	30	35	40	15	60		30	+27	40	35	40	50	50	50	70	80	50	0
5/31/40	40	30	35	45	45	15	(co 60	ld)	35	+22	40	40	45	50	50	50	45	75	48	+2
6/20/40	35	20	35	45	45	15	65	75	35	+22	40	30	40	45	45	45	55	75	45	+5
7/26/40	35	25	30	35	40	20	55	80	32	+25	40	35	45	45	50	50	65		48	+2
8/10/40	35	30	35	45	40	20	60		35	+22	40	35	40	50	50	50	65	75	50	0
8/25/40	30	20	30	25	30	15	70		23	+34	45	30	40	45	50	45	80		47	+3
9/21/40		20	25	30	30	15	65		25	+33		35	40	45	45	45	60	80	45	+5
10/1/40		25	30	35	35	20	60		30	+27		35	45	45	45	50	70		47	+3
10/19/40	30	20	20	25	30	20	60		25	+32	35	30	40	45	45	45	80		45	+5
11/23/40	30	20	25	30	30	15	60		25	+32	30	20	35	45	50	45	80		47	+3
12/23/40	25	25	30	30	30	15	60		25	+32	30	25	35	45	45	50	90		47	+3

1. Enchondralization of the fenestra. By this we mean exposing the osteogenetically inert enchondral layer of the bony labyrinthine capsule as widely as possible beyond the margins of the fenestra. This is accomplished by removing the osteogenetically more active periosteal layer, leaving the fenestra on top of a dome-shaped mound.

2. Scrupulous removal of all bone chips and bone dust particles from the region of the fenestra by means of: (a) the use of continuous irrigation while making the fenestra, (b) careful search with the binocular loupe for bone chips on the periosteal surface of the tympanomeatal skin flap, (c) the use of adequate magnification with the binocular microscope to remove the endosteum with its adherent bone particles from the mouth of the fenestra.

3. Avoidance of trauma to the endosteum within the margins of the fenestra, by using adequate magnification with the binocular operating microscope while removing the endosteum from the mouth of the fenestra.

4. Thorough burnishing of the bone around the fenestra with the 14 karat hard gold burnishing burr.

5. Avoidance of bleeding into the perilymph space by: (a) strictly local anesthesia, (b) continuous irrigation, (c) reinspection of the fistula after the flap has been in place for a short time to be sure there is no active bleeding under the flap at the completion of the operation.

During the past year the technique developed by us at Northwestern University has incorporated 2 features to decrease cochlear damage from postoperative serous labyrinthitis: (1) elastic absorbent sponge packs kept under continuous pressure against the tympanomeatal skin flap for 6 days, (2) immobili-

TABLE III.—STATISTICS ON 415 CASES TESTED 2 YEARS OR MORE AFTER OPERATION

(Nov-Ovalis with Enchondralization, Irrigation and Microscope)

	No.	Per cent
No change	18	4.3
Further loss	7	1.7
Improved more than 11 decibels	390	94
Gain subsequently lost	12	2.9
Gain partly lost	15	3.6
Gain fully maintained	363	87.5
Breakdown of 390 Cases Improved		
Gain subsequently lost	12	3
Gain partly lost	15	3.8
Hearing fully maintained		
Total	363	93
+11 to +19 decibels	58	14.7
+20 to +29 decibels	126	32.3
More than +30 decibels	179	45.9
30 decibels practical level	197	50.5

Statistical analysis of probably permanent hearing results in all patients operated upon by the Northwestern University improved fenestration technique.

TABLE IV.—STATISTICAL ANALYSIS OF 300 CASES IN WHICH PATIENTS WERE OPERATED UPON BY THE IMPROVED FENESTRATION TECHNIQUE INCLUDING FEATURES TO DECREASE POSTOPERATIVE SEROUS LABYRINTHITIS

January 1946 to September 1946

	No. of cases	30 db pract. level	Average db gain	Improved 10 db or more	Unchanged less than 10 db	Worse 10 db or more less
Class A ideal	183	83.6%	28 db	96.2%	3.3%	0.5%
Class B guarded prognosis	62	46.8%	30.9 db	90.3%	8.1%	1.6%
Class C experimental	55	18.1%	30.4 db	82%	18%	0%
Total cases	300	64%		92.3%	7%	0.7%

zation of the cochlea for 6 days by a head-frame to prevent it from being dependent to the fistula.

With this technique the incidence of bony closures has been reduced to less than 5 per cent of cases tested 2 years or more after operation (Table III). During the past year the incidence of postoperative serous labyrinthitis has been materially reduced (Table IV) with a definite gain in the hearing results. The final results with the sponge and head-frame technique must await the passage of at least 2 years.

HOW DOES THE HEARING AFTER OPERATION COMPARE WITH A HEARING AID?

The third question is: How does the operation compare with a hearing aid? One otologist stated that a hearing aid will do as much or more for the hearing without the discomforts, risks, uncertainties and expense of surgery. However, we have found that many patients who have had the fenestration operation and who regard the results as satisfactory, assert without qualification that they hear better now than they did with their aid, and without the distortion, the nuisance, and the upkeep expense of an aid. One patient writes: "The ear phone is a poor substitute for normal hearing. If this seems too obvious a statement, it is only that I, who have been through the looking glass of the distorted and undistorted reflection, can hardly believe my ear now that it has been given back to me."

To try to compare a hearing aid with the operation by objective tests, 3 years ago we carried out speech reception tests in terms of decibels on patients with their hearing aid before operation and without their aid after operation. Even in cases in which the postoperative hearing did not reach the 30 decibel practical level we found that 7 patients who received a gain of more than 20 decibels for the speech frequencies understood speech better after the operation than they could before with their hearing aid. These tests may not have been entirely fair to the hearing aid, however, since a patient about to undergo the operation is not likely to invest in a new improved hearing aid. Further and more exact studies of this sort are now being made by Dr. Carhart, of the Northwestern University School of Speech. The patients are being tested before operation with a well-fitted hearing aid and the hearing for speech compared with the hearing after operation.

CAN OPERATION ARREST OR PREVENT THE NERVE DEGENERATION OF OTOSCLEROSIS WITH STAPES ANKYLOSIS?

The fourth question concerns the effect of the operation, if any, on the nerve degeneration of otosclerosis. This very important ques-

tion we cannot as yet answer with certainty. We can, however, make the following statements:

In cases followed for 5, 6, and 7 years after operation, where the fenestra remains open with a sustained hearing improvement, further nerve degeneration in the ear operated upon has rarely been observed, even when nerve degeneration had already begun at the time of operation.

When the fistula has closed, with loss of the hearing improvement, nerve degeneration in the ear operated upon has continued to progress.

In a few cases with definitely progressive nerve degeneration in the ear not operated upon the ear operated upon has failed to show any evidence of further nerve degeneration.

We have reason to hope, therefore, that the fenestration operation may, in some as yet unexplained way, arrest or prevent the secondary nerve degeneration of stapes ankylosis, at least in some cases. The final answer to this important question must await further observations on a large number of patients successfully operated upon over another 5 to 10 years.

WHAT ARE THE RISKS?

The fifth question of the risks of the fenestration operation can be answered as follows: In more than 1300 consecutive fenestration operations, plus 39 revisions, carried out by myself and my associate, Dr. Juers, we have had no deaths and no serious infections.

The most frequent complication is transient facial paralysis coming on about 1 week after operation with complete recovery a few weeks later. This paralysis has occurred in 3 per cent of our operations. In 3 cases recovery was incomplete after 1 year, but in no case did a complete paralysis remain.

Femoral phlebitis occurred in 4 patients during the first 2 weeks after operation, with a pulmonary embolus in one. All recovered. To prevent this complication, active and passive leg exercises are now a routine procedure in all cases.

Postoperative pulmonary atelectasis occurred after one of the early operations in which ether was used (Case 15). The patient recovered.

Schizophrenia, probably incipient before operation, became manifest after operation in one of the early cases (Case 23).

The chief danger of the operation is permanent damage to the labyrinth, and particularly to the cochlea, with persistent dizziness or with permanent depression of hearing below the preoperative level.

Dizziness sufficient to be annoying as a rule clears up within a few weeks. Rarely it lasts as long as 2 years. In only 1 case has it lasted more than 2 years; this patient complains of persistent ataxia and unsteadiness while walking 2½ years after operation.

Permanent depression of hearing below the preoperative level has occurred to date in 37 operations (2.9 per cent of all patients operated upon) and in 1 of the 39 revisions.

HOW PERMANENT ARE THE HEARING IMPROVEMENTS?

The last question to be answered in evaluating the usefulness of the fenestration operation concerns the permanency of the hearing improvements.

Otologists who opposed the fenestration operation in its early stages of development did so on the grounds that the hearing improvements would never last because sooner or later bony closure of the fenestra would surely occur. As the result of animal experimentation, and of clinical observation in many patients successfully operated upon and followed for more than 5 years, we may now affirm what we previously hoped, and that is that once healing has become complete osteogenesis tending to close the fistula ceases, and a fistula still open may be expected to remain open permanently. In the monkey, healing is complete and active osteogenesis has virtually ceased 3 or 4 months after operation in most cases. In the human, bony closure occurs mostly during the first postoperative year, occasionally during the second postoperative year, and almost never later than 2 years after operation. A hearing improvement maintained for 2 years after the fenestration operation may be regarded as almost certainly permanent. Study of the hearing of patients successfully operated upon and followed for 5 years or longer shows how the improvement is

generally maintained without significant variations year after year. In some cases the greatest hearing improvement occurred 6 months after operation, with subsequent hearing tests slightly lower, indicating partial narrowing of the fenestra. After the second year, however, osteogenesis has ceased and the hearing improvement is maintained at a stationary level.

The ultimate fate of the hearing improvements 10, 20, and 30 years after the fenestration operation must await the passage of time. From our experience to date we are justified, I believe, in assuming that the 2 year hearing results are permanent.

An evaluation of the fenestration operation includes a consideration of its limitations and shortcomings.

First, there is the fact known to all otologists, but unfortunately not stressed in lay articles, such as appeared in *Hygeia* and the *Reader's Digest*, that the fenestration operation virtually never restores the hearing to normal. The operation may be expected to restore about half the hearing that has been lost, provided the patient is suitable for operation.

Second, the results of the operation in any case continue to be unpredictable. With the best of preoperative indications, and the best of operative techniques, failures still occur in some cases.

Third, the fenestration operation is technically difficult to learn and its results will vary more with the skill and experience of the individual surgeon than do most operations. The question of training and perhaps certifying fenestration surgeons is a difficult problem that needs attention.

Finally, the fenestration operation is a strictly elective procedure. A hearing aid may always be resorted to in cases which are not suitable or in which surgery is hazardous on account of age, health, or nervous instability.

CONCLUSIONS

In our evaluation of the present status of the fenestration operation, we have sought answers to 6 questions, as follows:

1. The operation is useful in two types of cases: The ideal case with stapes ankylosis and normal cochlear function where we may expect to restore practical hearing; the suitable, but not ideal case with stapes ankylosis and slightly impaired cochlear function where we may hope to gain enough hearing so that the patient can go without his hearing aid.

2. The judgment as to which technique is the best must await the publication of adequate detailed statistical data. The results obtained by us with the technique developed at Northwestern University Medical School are presented.

3. Subjectively, most patients prefer the hearing after operation to a hearing aid, and 82 per cent of cases operated upon by us regard the operation as successful and do not use a hearing aid. Preliminary objective tests seem to confirm the fact that patients who experience an average improvement generally understand speech better than they did with their aid before operation.

4. There is evidence that a successful fenestration operation may arrest or delay the nerve degeneration of otosclerosis in some cases, but it is too early to be certain of this.

5. With a meticulous aseptic technique the risks of the fenestration operation have proved to be minimal. The chief risks are to the facial nerve and to the labyrinth.

6. The 2 year hearing results of the fenestration operation may be regarded as the permanent hearing results.

THE USE OF RADIUM IN THE TREATMENT OF CONDUCTIVE DEAFNESS

JOHN E. BORDLEY, M.D., Baltimore, Maryland

IRRADIATION of the nasopharynx with radium or with radon is effective in the treatment of that type of conductive deafness which is due to obstruction of the pharyngeal end of the eustachian tube by lymphoid tissue. It is not effective in the treatment of other forms of deafness. This treatment is more effective when instituted early, before inflammatory reactions and infections of the mucosa of the middle ear have progressed to the stage of fibrous fixation of the ossicles.

Persons with conductive deafness, whatever the cause, hear better by bone conduction than by air conduction (i.e., the Rinne test is negative), and they usually have good hearing by bone conduction. The impairment shown by means of the air conduction audiogram may be essentially "flat" or may be considerably "tilted" in the high or in the low tone ranges.

Conductive deafness results from any condition that seriously interferes with the transmission of air-borne sound waves to the inner ear. The common causes of conductive deafness are lesions that interfere with normal movements of the middle-ear ossicles. On the basis of pathology, three subdivisions may be made of the common lesions that interfere with ossicular mobility. The first is ankylosis of the footplate of the stapes by otosclerosis (Fig. 1); this is an irreversible lesion. The second is fibrosis of the mucosa of the middle ear to such an extent that normal movements of the ossicles are prevented by dense fibrous adhesions (Fig. 2); such lesions also are irreversible. The third common type of lesion, the one present during the early period of tubal obstruction, is reversible, and is the one that can effectively be treated by irradiation of the nasopharynx.

From the Otological Laboratory of the Johns Hopkins University School of Medicine.

Presented before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–20, 1940.

The essential difference between the third type of lesion and the second type is the structure of the mucosal thickenings that interfere with ossicular movements. In tubal occlusion the mucosa is edematous and hyperemic, due to the negative pressure in the middle ear caused by lack of replacement of the air absorbed by the moist walls of the closed cavity. Only after the condition has persisted for a long time and has been aggravated by repeated low-grade infections does fibrosis of the edematous mucosa occur to a degree sufficient to interfere permanently with ossicular movements. So long as the thickening of the mucosa is primarily edematous, the lesion is reversible if normal aeration of the middle ear can be restored.

Unfortunately, it is not possible to present sections of ears which have received irradiations for conductive deafness, because none of our patients has come to autopsy. The next two illustrations, however, show what takes place in ears where there has been such failure in function of the eustachian tube. The first section (Fig. 3) is from the ear of a patient who had repeated attacks of otitis media and deafness. At the time of death her hearing was within normal limits. Her tympanic membranes were scarred and retracted, and as the sections show, the middle ear has a greatly thickened tympanic membrane and the mucous membranes are thickened and infiltrated with inflammatory cells. The second section (Fig. 4) is from a 16 year old boy with normal hearing. Otoscopic examination showed marked retraction of the tympanic membrane. The sections illustrate minimal changes with some thickening of the tympanic membrane and definite thickening of the mucous membranes of the middle ear, especially over the promontory. Neither of these cases shows irreversible changes around the ossicular chain. It is quite easy to visualize how the first case could develop deafness when further

swelling took place and secretions became backed up into the tympanic cavity.

The selection of patients suitable for treatment with radium can only be done with any accuracy by taking into consideration the history, the otoscopic examination, the nasopharyngoscopic examination, and hearing tests. A very careful history must be taken. Fluctuating hearing and hearing much affected by upper respiratory tract infections or by changes in altitude or humidity are some of the common symptoms. Occasionally, there is a history of frequent attacks of otitis media or a feeling of fullness in the ears. These symptoms are not necessarily bilateral. There does not have to be a history of mouth breathing. The deafness is usually progressive over a long period of time in spite of its fluctuations. The otoscopic examination may reveal a slightly thickened and retracted tympanic membrane, some retraction of Shrapnell's membrane, and a fluid level or the "chicken wire" appearance of mucous bubbles behind the tympanic membrane. The nasopharyngoscopic examination most frequently reveals hypertrophied lymphoid tissue in the fossa of Rosenmueller and around the eustachian orifice. Figure 5 illustrates a normal eustachian orifice which can be compared with one covered by such an overgrowth of lymphoid tissue (4). Occasionally, very little more than congestion or mucoid discharge can be seen around the orifice. Hearing tests made with the audiometer and tuning forks are necessary to establish the diagnosis of conductive deafness. The audiograms usually contribute very little toward a differential diagnosis except in those few early cases which show an exaggerated high tone loss superimposed on the usual flat loss. About half of our patients show equivocal or just negative Rinne tests, with a 512 d.v. tuning fork.

Radium emanations are employed in the nasopharynx to reduce the amount of lymphoid tissue and combat the chronic infections involving the pharyngeal end of the eustachian tube (1). It is this tissue which acts as a focus of infection pointing toward the middle ear and likewise acts as a mechanical obstruction to the proper drainage and aeration of the middle ear. The backing up of infected secretions into the middle ear results in a low-grade inflammation with edema of the membranes and excessive secretions. In time, this obstruction of the tube builds up a negative pressure within the tympanic cavity and causes retraction of the tympanic membrane. Such changes result in interference to the normal movement of the ossicles and a conductive type of hearing loss. Such conditions, if allowed to persist, lead to the formation of scar tissue and a permanent limitation of ossicular movement. The nasopharynx, then, is the danger spot that must be treated to relieve the symptoms of reversible conductive deafness. It is just as important to clear up the infection as to remove the mass of the tissue itself. Use of antibiotics in conjunction with irradiation is definitely indicated in some cases. Radium has been chosen by our clinic, first, because as Heineke showed in 1905 lymphoid tissue is highly sensitive to irradiation, and second, because it offers a means of applying such rays locally in high concentrations without first passing them through normal surrounding tissues in which many of them will be absorbed. Thus, the maximum dose can be delivered at the desired point and the possibility of injuring surrounding structures reduced. The action of radium is on the germinal centers of the lymphoid tissue. Also, Burnam in a personal communication states that radium has a powerfully destructive effect upon the bacteria growing within this tissue.

To obtain maximum results, it has usually been necessary to administer repeated treatments with radium. We now use a series of three irradiations spaced 2 weeks apart. The dose used is calculated at 25,000 milligram seconds for the standard monel metal Army applicator or 17,000 millicurie seconds for the stainless steel radon gas applicator made by the Kelly Clinic. This difference in the calculated doses is due to the larger proportion of β rays that pass through the stainless steel. Both applicators are applied by simply inserting them along the floor of the nostril into the nasopharynx in close proximity to the eustachian orifice. Thousands of irradiations have been given in our clinic with no single serious reaction. Likewise, no serious reaction followed any of the 14,000 treatments given in the

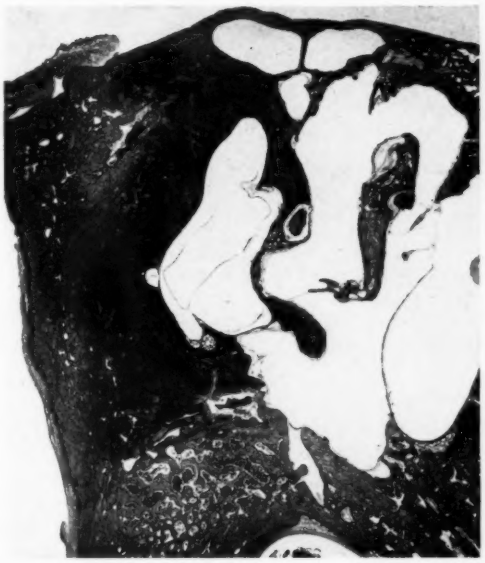

Fig. 1. Photomicrograph of a section through the middle ear of a 47 year old man with a history of conductive deafness. The middle ear is normal except for the otosclerotic process involving the footplate of the stapes.

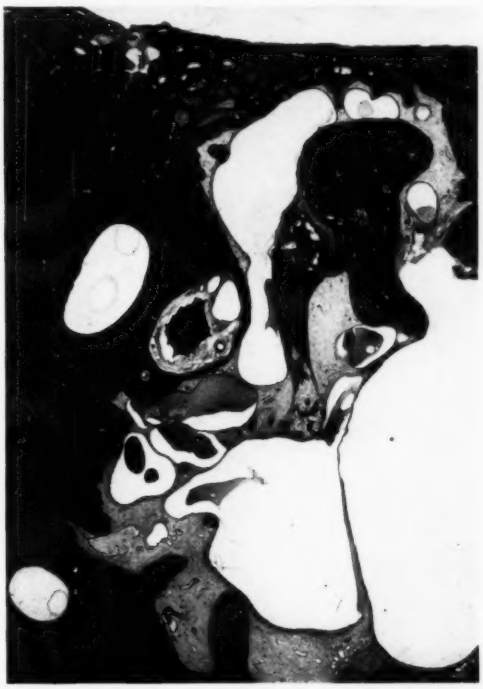

Fig. 2. Section through the middle ear of a 36 year old man. The heavy fibrosis around the malleus and incus, and in the attic, illustrates an irreversible type of lesion causing conductive deafness.

Army Air Forces aerotitis control program (6). The efficacy of such treatment to remove lymphoid obstruction of the eustachian tube and restore its normal function has been conclusively proven in the well controlled experiment recently reported by Haines and Harris. They irradiated a group of sailors who had been rejected as candidates for the Submarine Training School because they had developed aerotitis media during the pressure tests required in submarine escape training. Ninety per cent of this treated group were subsequently able to equalize middle ear pressure on repetition of the tests. Ninety per cent of the control group which had received only symptomatic treatment recontracted aerotitis media when they were again subjected to pressure changes.

It has been found that in conductive deafness of the reversible type the treatment must be given early (2). It must be given before scar tissue begins to form if good results are to be obtained. Patients with large central masses of adenoids should have them removed surgically before irradiation. This allows more direct application of the rays to the fossa of Rosenmueller, the eustachian orifice, and Gerlach's tonsil.

Best results have been obtained in children. As a group, children have less connective tissue than do adults in the lymphoid tissue of the nasopharynx. Many adults with this clinical picture have had a long standing intermittent subclinical eustachian obstruction with recurrent mild middle ear inflammation which has resulted in the gradual formation of scar tissue around the ossicles. In the children's series about 45 per cent of those selected for treatment of conductive deafness have shown appreciable, useful increase in hearing acuity. Not over 25 per cent of adults show such improvement. It is felt that this difference in improvement is because of inability accurately to tell how much permanent ossicular interference is present, and that if otologists are even-

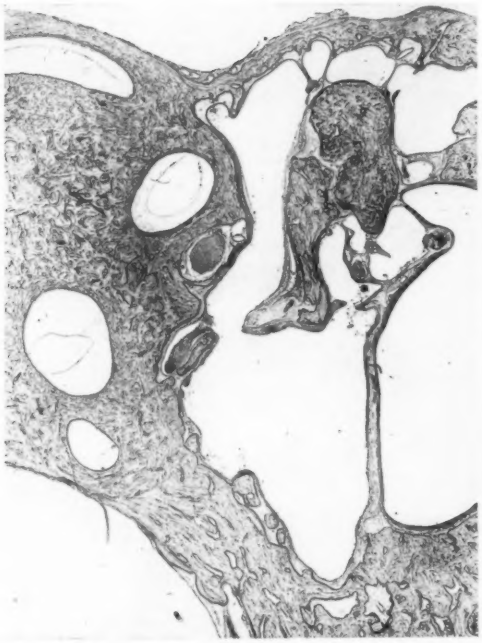

Fig. 3. Section showing fibrosis around the ossicles, a thickened tympanic membrane, and edema of the mucous membranes of the middle ear. This section is from a 37 year old woman with a history of reversible conductive deafness but with normal hearing at death.

Fig. 4. The middle ear of a 16 year old boy, showing thickened mucous membranes over the promontory and slight fibrous thickening of the tympanic membrane. The hearing was normal when it was tested during his final illness.

tually able to determine this, the incidence of good results will show a marked increase.

Two cases have been chosen to illustrate reversible conductive deafness and what may happen when irradiation therapy is given. The first case (Fig. 6) is a boy aged 9, one of identical twins, who had begun to fail in school and who had a speech defect. He was thought to be mentally defective. His identical twin was leading the first division of this child's class. This child had had two adenoidectomies and a tonsillectomy. At times his family felt he had some deafness. There was no history of previous ear trouble. His tympanic membranes were severely retracted, with scarring of Shrapnell's membrane. A mass of adenoids in the nasopharynx had completely overgrown the eustachian orifices. The bone conduction was excellent; the Rinne test was negative on both sides. An adenoidectomy was performed with no change in his hearing. At the end of July he received his first irradiation and shortly afterward began to improve. By January his hearing was much improved (Fig. 6, second audiogram). His Rinne had become positive. Within 1 year his speech defect disappeared and he was with his twin in the first division of his class.

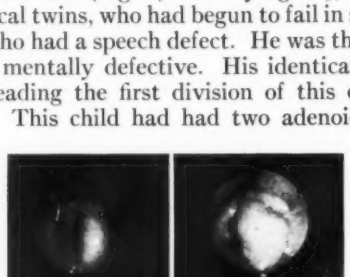

Fig. 5. Photographs made through a nasopharyngoscope showing, left, a normal eustachian orifice and, right, a eustachian orifice overgrown with lymphoid tissue. (From Hendricks and Lieberman 4.)

The second example (Fig. 7) is a 12 year old boy who had been deaf since infancy, but the family had noticed a marked fluctuation of his hearing with colds. He had had no otitis.

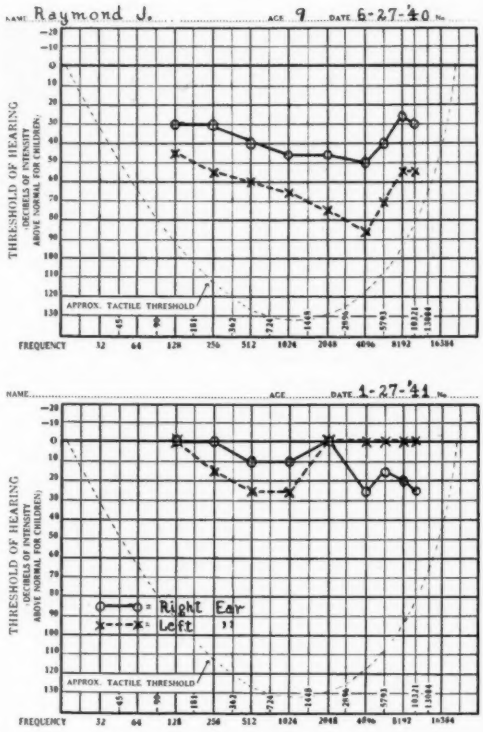
NAME Raymond J. AGE 9 DATE 6-27-40
THRESHOLD OF HEARING
DECIBELS OF INTENSITY
ABOVE NORMAL FOR CHILDREN
APPROX. TACTILE THRESHOLD
FREQUENCY
32 64 128 256 512 1024 2048 4096 8192 16384
NAME AGE DATE 1-27-41
O = Right Ear
X = Left "

Fig. 6. Audiograms showing hearing improvement which was gained in a 9 year old boy 5 months after first irradiation treatment of eustachian orifices was administered for conductive deafness.

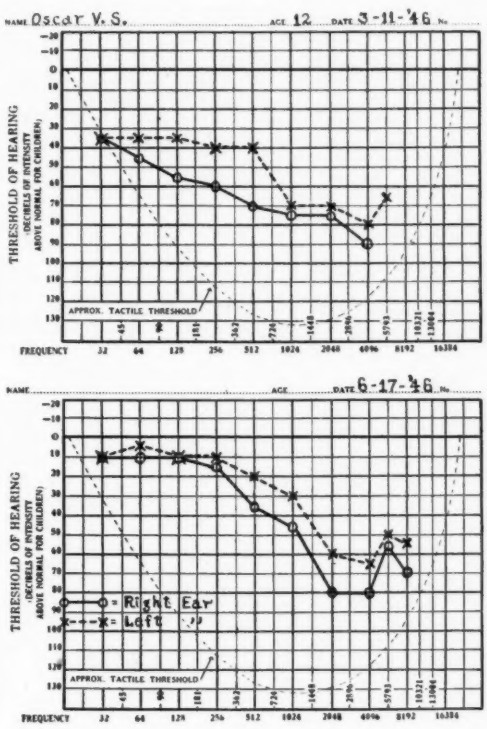
NAME Oscar V. S. AGE 12 DATE 3-11-46
THRESHOLD OF HEARING
DECIBELS OF INTENSITY
ABOVE NORMAL FOR CHILDREN
APPROX. TACTILE THRESHOLD
FREQUENCY
32 64 128 256 512 1024 2048 4096 8192 16384
NAME AGE DATE 6-17-46
O = Right Ear
X = Left "

Fig. 7. These audiograms illustrate the improvement in hearing resulting from treating a conductive lesion which was superimposed upon a congenital nerve deafness. In this case, bone conduction remained poor.

The tympanic membranes were dusky in color, not retracted. The eustachian orifices were peppered with lymphoid nodules. His hearing showed an accentuated high tone loss. Bone conduction was shortened on both sides, but the Rinne test was negative on both sides. Following irradiation, it could be seen that he had nerve deafness with a typical Manasse type curve in his audiogram (Fig. 7, which had been depressed by a superimposed conductive lesion. His Rinne test became positive, but he still had a shortened bone conduction.

CONCLUSIONS

The use of radium or radon offers an important additional type of therapy in the otologist's struggle against deafness. Like other methods of treatment, however, it has definite limitations, and in order that its usefulness may be realized, radium must be used within these limits. Treatment of deafness due to permanent ossicular fixation with radium is just as futile as doing a fenestration operation on a patient with no bone conduction. The key to the successful employment of radium is the careful and correct selection of cases. The history is as important as the examination. The earlier a patient is treated, the better are the chances for improvement. The younger the patient, the more effective the irradiations will be. It is important to remember that radium treats the cause of eustachian obstruction and infection. It does not treat connective tissue lesions in the middle ear. It is effective in the nasopharynx, not at the oval window niche or the attic.

The danger to the future of radium therapy is in its overenthusiastic use by otologists not willing to take the care and the time to study each individual case. The indiscriminate use of this technique may bring it into disrepute. Its future is bright if we remember that a great number of patients lose their hearing each year as a result of nasopharyngeal infection and lymphoid hyperplasia, and it was for the prevention of such deafness that the radium applicators were first designed.

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CONSIDERATION OF HEARING IMPAIRMENT IN THE TREATMENT OF CHRONIC SUPPURATIVE OTITIS MEDIA

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THE degree of hearing impairment associated with chronic middle ear suppuration varies greatly in individual cases. The amount of damage done to the middle and internal ear structures by acute infection at the onset, the extent of bone necrosis, and the interference with the sound conduction mechanism of the middle ear resulting from the healing process influence the loss of hearing acuity. There may be a conductive type of hearing loss of mild or severe degree, a mixed type of deafness if there is associated cochlear damage, or, in some instances, a profound nerve deafness.

In the management of middle ear suppurations, the improvement of hearing or, at least, the preservation of residual hearing usually is not the major problem. The otologist is more concerned about the dangerous potencies of the infection from the standpoint of possible extension into the otic capsule or intracranial cavity. The patient's chief concern is more often associated with the annoying malodorous discharge. Although the hearing loss may not be the most important aspect of a case of chronic middle ear infection, it is not a factor to be ignored. In the case of bilateral middle ear disease, the hearing loss may be of tremendous importance to the patient who may have to go through a complete rehabilitation program if further hearing impairment should develop.

How then should the otologist consider the problem of hearing impairment in his management of chronic middle ear suppurations? This question can be answered, I believe, by stating that first consideration should be given to the determination of the extent and dangers of the infection. Then, other factors being equal, the treatment advocated should be that which will, while dealing adequately with the infection, tend to preserve all residual hearing or even improve the patient's hearing acuity. This can be accomplished only by individualizing each case and adapting the therapeutic procedure to the individual patient. Many of us will agree that there has been a tendency to use rather routinely some form of drops or powder as "conservative treatment" in cases of chronic otitis media. Then if the ear does not stop discharging, a radical mastoidectomy is considered. Too many times this conservative form of neglect has been continued until intracranial extension of the infection has ensued. This form of treatment suggests that deplorable practice of adapting the patient to a routine therapeutic procedure.

In discussing individualized treatment from the standpoint of preservation of hearing, it is necessary that we understand the various major types of chronic suppurative otitis media and that we be able to recognize them clinically. It would be absurd, for instance, to use the same routine type of treatment in a case of so-called "tubal ear" as in a case of attic cholesteatoma. In each instance, however, the patient may complain only of moderate hearing loss and chronic discharge which may be continuous or intermittent.

The first uncompromising demand then, in the management of a case of chronic suppurative otitis media, is a thorough and painstaking clinical examination.

The history should, if possible, reveal facts regarding the onset of the discharge. It is well to know if the infection began before the age of complete pneumatization of the mastoid, if the infection originally complicated measles or scarlet fever, or if the onset was insidious. One should ascertain any unusual symptoms accompanying acute exacerbations and bear in mind that intracranial complications usually develop during such recrudescences. The history of these episodes should reveal information relative to the typical danger signs of such

From the Department of Otolaryngology, University of Michigan Medical School.

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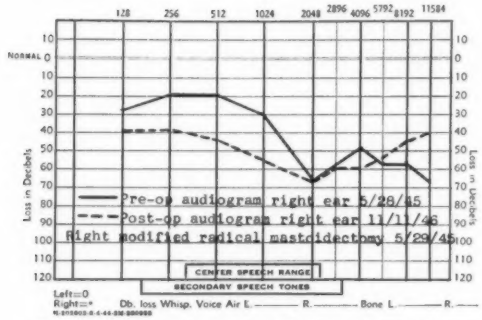
128 256 512 1024 2048 2896 4096 5792 8192 11584
NORMAL 0
Loss in Decibels
Pre-op audiogram right ear 5/28/45
Post-op audiogram right ear 11/11/45
Right modified radical mastoidectomy 5/29/45
CENTER SPEECH RANGE
SECONDARY SPEECH TONES
Left=0
Right=•
Db. loss Whisp. Voice Air L. R. Bone L. R.

Fig. 1. Audiogram in patient W. E. aged 22 years.

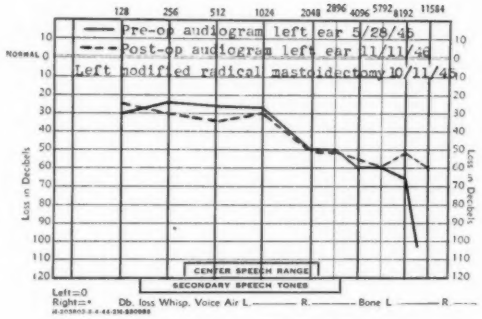
128 256 512 1024 2048 2896 4096 5792 8192 11584
NORMAL 0
Loss in Decibels
Pre-op audiogram left ear 5/28/45
Post-op audiogram left ear 11/11/45
Left modified radical mastoidectomy 10/11/45
CENTER SPEECH RANGE
SECONDARY SPEECH TONES
Left=0
Right=•
Db. loss Whisp. Voice Air L. R. Bone L. R.

Fig. 2. Second audiogram in patient W. E.

infection. These general signs and symptoms which have no place in a case of uncomplicated chronic suppurative otitis media and mastoiditis are as follows: (1) hemicrania or generalized headache, (2) chills, (3) convulsions, (4) changes in sensorium, (5) extraocular muscle palsies, (6) vertigo, (7) nausea and vomiting, (8) leucocyte count over 20,000 in adults, and (9) marked disproportion of symptoms and signs. The existence of these signs past or present usually suggests an infection of serious nature.

Physical examination should include a complete and detailed study of the nose, nasopharynx, throat, and ears. The significance of the various types of perforations in the drum membrane and the various types of discharge must be understood by the otologist.

The therapeutic management should depend upon the position and extent of pathological changes present and upon the likelihood of extension of infection to the fallopian canal, the inner ear, or the intracranial contents. This information must be obtained from the clinical examination and not from an X-ray report only.

In the typical "tubal ear," demonstrating an anterior inferior perforation and a mucoid discharge, the hearing loss is usually not profound, and if the ear becomes dry with concomitant thinning of the hyperplastic tympanic mucosa, the hearing is likely to improve. Since the major pathologic changes are hyperplasia, edema, and round cell infiltration in the tympanic mucosa, one need not be concerned immediately about the possibility of mastoid complications. Treatment should be directed first to the nasopharynx from which hypertrophic adenoid tissue should be removed. In many instances the application of radium to the region of the eustachian tube orifices will have a beneficial effect. The local treatment to the ear should have cleanliness as its chief objective. Antiseptic solutions may be instilled daily by the patient. A saturated solution of boric acid in 70% alcohol used as ear drops is of value.

If there is fairly good evidence that the mastoid inflammation is minimal and that the tympanic mucosa is intact but secreting an abundance of mucus, x-ray therapy is often of considerable value. The prognosis on such conservative treatment is good even though there may be recurrence of the discharge during upper respiratory infections.

In the case of the large marginal perforation with granulations on the promontory but without granulation tissue or cholesteatome in the attic, there is, of course, hearing loss; but if the ossicular chain is intact and the region of the stapedial footplate is free from granulation tissue, the hearing loss is usually around 30 to 40 decibels, a level of rather serviceable hearing. In such an instance conservative local treatment may be continued indefinitely. The granulation tissue should be removed with great care after which the patient should be instructed to use local medication in the form of drops or powder of antiseptic, antibiotic, or digestive material.

The presence of a posterosuperior marginal perforation associated with foul smelling seropurulent discharge, and cholesteatome or granulation tissue filling the attic indicates an in-

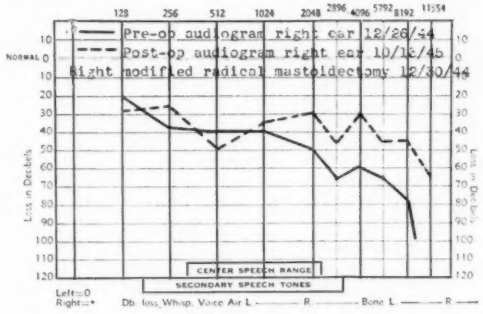
128 256 512 1024 2048 2896 4096 5792 8192 11584
Pre-op audiogram right ear 12/26/44
Post-op audiogram right ear 10/12/45
Right modified radical mastoidectomy 12/30/44
NORMAL 0
Loss in Decibels
CENTER SPEECH RANGE
SECONDARY SPEECH TONES
Left=0
Right=•
Db. loss Whisp. Voice Air L. R. Bone L. R.

Fig. 3. Audiogram in patient B. M., aged 22 years.

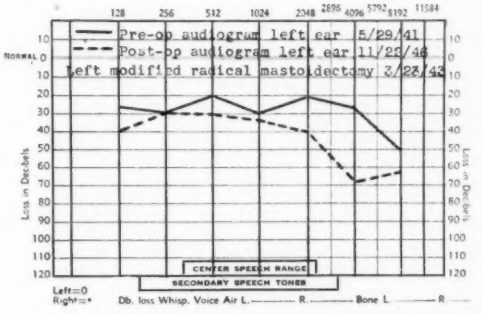
128 256 512 1024 2048 2896 4096 5792 8192 11584
Pre-op audiogram left ear 5/29/41
Post-op audiogram left ear 11/22/46
Left modified radical mastoidectomy 3/28/42
NORMAL 0
Loss in Decibels
CENTER SPEECH RANGE
SECONDARY SPEECH TONES
Left=0
Right=•
Db. loss Whisp. Voice Air L. R. Bone L. R.

Fig. 4. Audiogram in patient O. A., aged 28 years.

fection of serious potentialities. The ossicular chain usually has been interrupted by necrosis of its component parts. The stapes or perhaps only its remaining footplate may be embedded in a mass of scar and granulation tissue. This type of otitis media is associated in most instances with bone necrosis, granulation tissue and perhaps cholesteatome formation in the tympanic antrum and neighboring mastoid cells. Hearing loss is greater than in the preceding type. Usually there is a loss of at least 50 or 60 decibels. In such a condition conservative therapeutic measures are of little value since the pathologic changes are deep seated. Radical mastoidectomy is frequently indicated, and this operation must be a precision type of procedure in which all diseased tissue is removed. One should expect to obtain complete healing in over 95 per cent of adult cases. The hearing will not be restored, but it may be improved slightly, 10 decibels or so, if there is a large mass of granulation tissue in the middle ear before operation and if after healing the mesial wall of the tympanum becomes covered by thin skin. If there is but little granulation tissue in the region of the stapes before operation, and after healing the promontory and region of the stapes is covered by a thick layer of scar, the patient will suffer some increase in hearing loss. Occasionally a radical mastoidectomy may produce total loss of hearing in the ear operated upon. However, if the disease is of such severity and extent that a radical mastoidectomy is indicated, one should not procrastinate for fear the required operation may add to the patient's hearing impairment. To do so invites intracranial complications. There is at least an even chance of preserving the residual hearing and this chance must be taken even if the disease is bilateral and of sufficient severity and extent to demand bilateral radical mastoidectomies. Too many times patients have been permitted to develop severe complications while a useless conservative medical form of treatment is being given a prolonged trial. The extension of infection along a pathway created by bone necrosis or by pressure atrophy due to cholesteatome formation, takes place insidiously. The lack of pain or other untoward symptoms gives the physician a false sense of security while continuing the medical therapy. One must bear in mind the fact that the indications for radical mastoidectomy are present and must be discovered *before* a complication occurs. When the patient who has an old chronic suppurative otitis media develops a labyrinthitis, sinus thrombosis, facial paralysis, meningitis, or brain abscess the physician knows, and perhaps too late, that he should have recognized the indications for operation weeks, months, and perhaps even years before. Increasing hearing loss, profuse foul seropurulent discharge, and episodes of pain and mastoid tenderness in a case of chronic otitis media almost always mean extending infection and impending complications. Mastoid tenderness is a most important sign of severe extending infection in the case of a small sclerotic mastoid. Roentgenograms should be made, of course, and they are of great value if well exposed and expertly interpreted; but the indications for operation are to be discovered in the clinical examination.

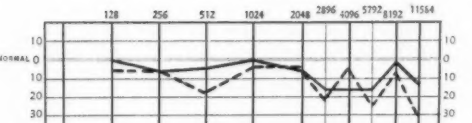
128 256 512 1024 2048 2896 4096 5792 8192 11584
NORMAL 0
Loss in Decibels
Pre-op audiogram left ear 5/24/43
Post-op audiogram left ear 9/13/43
Left modified radical mastoidectomy 6/7/43
CENTER SPEECH RANGE
SECONDARY SPEECH TONES
Left=0
Right=•
Db. loss Whisp. Voice Air L. R. Bone L. R.

Fig. 5. Audiogram in patient J. M., aged 17 years.

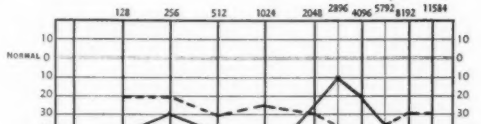
128 256 512 1024 2048 2896 4096 5792 8192 11584
NORMAL 0
Loss in Decibels
Pre-op audiogram right ear 3/6/46
Post-op audiogram right ear 9/24/46
Right modified radical mastoidectomy 4/30/46
CENTER SPEECH RANGE
SECONDARY SPEECH TONES
Left=0
Right=•
Db. loss Whisp. Voice Air L. R. Bone L. R

Fig. 6. Audiogram in patient M. G., aged 22 years.

Less common, but most important, particularly in this discussion of chronic suppurative otitis media in relation to hearing impairment, is the primary acquired form of cholesteatoma. There is apt to be a very small perforation in the flaccid portion of the tympanic membrane. There may be minimal and even unnoticed discharge except during exacerbations of the infection when there is characteristically a thin, foul smelling exudate. The attic contains a mass of cholesteatome which may surround the head of the malleus and the body of the incus. In old cases the cholesteatoma may extend through the aditus into the antrum or expand downward into the tympanic cavity. The membrana tensa may be intact and show normal landmarks. A gray, lusterless, somewhat bulging membrane may indicate the presence of cholesteatome in the lower portion of the tympanic cavity. The hearing acuity varies, of course, but in many cases in which the suppuration and mass of cholesteatome are confined to the region of the attic, aditus, and antrum there is less than 30 decibels of hearing loss. With the exception of those cases which are discovered at a time when only the attic is involved and which may respond to repeated attic irrigations, this type of infection must be treated surgically. Obviously the instillation of drops or the insufflation of powder will be futile. The standard radical mastoidectomy will serve to cure the infection, but will certainly cause an increase in hearing loss if the hearing in the involved ear is at a serviceable practical level. The operation of choice in such a case is a modified radical mastoidectomy. The atticomastoidectomy as described by Lempert has many advantages. This operation, which may be done by either the postauricular or endaural approach, permits of thorough excavation of the epitympanum after removal of the incus and amputation of the head and neck of the malleus. By severance of the tendon of the tensor tympani muscle, the drum membrane may be retracted to give adequate exposure of the lower portion of the tympanic cavity if this is required. Preservation of the tense portion of the drum membrane which forms part of the tympanomeatal flap to be turned into the mastoid cavity, assures the maintenance of a tympanic air space about a stapes which has not been disturbed. In well selected cases, one can expect to obtain a perfectly dry healed ear and to preserve the hearing at a serviceable level.

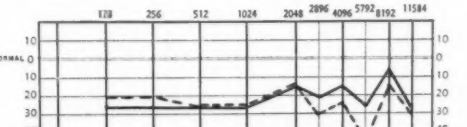
128 256 512 1024 2048 2896 4096 5792 8192 11584
NORMAL 0
Loss in Decibels
Pre-op audiogram, Right ear, 12/7/45
Post-op Audiogram, Right ear, 6/13/46
Right modified radical mastoidectomy 1/8/46
CENTER SPEECH RANGE
SECONDARY SPEECH TONES
Left=0
Right=•
Db. loss Whisp. Voice Air L. R. Bone L. R.

Fig. 7. Audiogram in patient N. C., aged 31 years.

Figures 1 to 7 demonstrate the preoperative and postoperative audiograms of patients on whom a modified radical mastoidectomy has been done for attic suppuration. In each case

the ear is dry and healed. One patient had the operation performed on both sides (Figs. 1 and 2). On the right side there was considerable loss of hearing after the operation but on the left side the hearing was preserved. Figures 3 and 4 show the hearing loss in 2 patients in whom it was essential that every effort be made to preserve the residual hearing. Each patient had previously undergone a radical mastoidectomy with loss of serviceable hearing in that ear.

SUMMARY

The management of the chronic suppurating ear is discussed from the standpoint of preservation of residual hearing. Although the amount of hearing loss in chronic middle ear suppuration is not the most important aspect of the disease, it is not a factor to be ignored. Treatment of chronic middle ear infections should be designed not only to deal adequately with the infection, but also, when possible, to preserve or even improve hearing. This can be accomplished only by individualizing the management of each case. The deplorable practice of attempting to adapt the patient to some routine form of conservative treatment is condemned. Intelligent treatment of such infections must be based upon knowledge of the type, extent, and severity of the pathological changes present; and this information must be gained from a thorough and painstaking clinical examination.

Some of the more important clinical types of chronic middle ear infection are described. Treatment of these conditions is discussed briefly and due consideration is given the associated problem of hearing impairment.

The modified radical mastoidectomy is recommended in selected cases of attic suppuration in order to avoid the greater hearing loss which would result from a classical radical mastoidectomy.

Preoperative and postoperative audiograms done on patients who have had a Lempert type of atticomastoidectomy are presented.

INDICATIONS FOR SURGERY IN THE LIGHT OF THE USE OF ANTIBIOTICS

HARRY P. SCHENCK, M.D., F.A.C.S., Philadelphia, Pennsylvania

THE indications for sinus surgery have become greatly modified during a single decade because widespread clinical trial has demonstrated the ability of the sulfonamides, and later, of the antibiotics, to modify profoundly the course of many acute and some chronic infections. Of the many known antibiotic substances only penicillin, streptomycin, and tyrothricin have attained a position of therapeutic importance. To each of these can be assigned a specific therapeutic sphere on the basis of accumulated laboratory and clinical data.

In the treatment of some infections the sulfonamides and the antibiotics supplement each other. The antibiotics cannot be regarded as entirely replacing the sulfonamides. Fortunately, the drugs of one or the other group may replace each other if the infecting micro-organisms develop resistant strains or the patient exhibits sensitization. The advantages of economy and plentiful supply of the sulfonamides are generally outweighed by the comparative safety and absence of toxicity of penicillin and streptomycin especially in extremely ill or debilitated patients with liver and kidney damage.

The definite reduction in the number of sinus operations performed in the United States during the past 2 years is attributed to the effective use of chemotherapy in acute and chronic infections as well as in certain types of traumatic fractures of the paranasal sinuses. On the other hand, the indications for surgical intervention in the presence of neoplasms or tissue alterations due to allergic phenomena have been little affected by the introduction of chemotherapeutic agents.

The antibiotics are of no value in uncomplicated allergy but they have been employed effectively against secondary infections complicating allergy of the upper and lower respiratory tracts. There is reason to expect therefore that bacterial sensitization may be forestalled in those instances where infection in an allergic individual can be arrested or eradicated by antibiotic therapy. On the other hand, allergic patients are prone to become sensitive to the antibiotic drug itself and this is especially apt to occur when the drug is administered as a prophylactic measure over a long period of time. Sinus surgery continues to be necessary in the presence of advanced, irreversible tissue changes in the nasal passages and sinus cavities if attributable to allergic influence alone and on the same basis as existed prior to the introduction of the antibiotics.

Certain advantages of properly applied antibiotic therapy are apparent during the preoperative period, the period of operation and the postoperative period of sinus surgery. In infectious sinus diseases, effective antibiotic therapy during the *preoperative period* depends upon early and accurate diagnosis (especially accurate bacteriological identification), followed by selection of the antibiotic most lethal to the invading micro-organism, given in adequate dosage by the most effective route of administration, and over a sufficient interval of time. Because antibiotic therapy frequently impedes or completely arrests the spread of infection, minimizes the occurrence of bacteriemia and the toxic effects of active and overwhelming infection, there is an appreciable prolongation of the "interval of safety" between the onset of symptoms and the need for surgical intervention. The value of such delay is obvious in providing the opportunity for more thorough and detailed clinical studies—roentgenological, serological, and bacteriological.

A sense of false security may be engendered by the prompt therapeutic effects of the sulfonamides and the antibiotics especially in sinus infections in which irreversible tissue reactions have already occurred. Here recurrence is the rule as soon as chemotherapy is with-

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drawn and although recurrent attacks may subside under further chemotherapy, eventual surgery is inevitable in the majority of patients.

The administration of antibiotics in mild and transient sinus infections may eventually be regarded as poor therapeutic practice. It has long been recognized that immunity fails to develop when infections are promptly controlled by chemotherapy. Prompt arrest of bacterial activity prevents stimulation of immunological responses. As a result there are frequent recurrences at very short intervals. The tendency to readminister chemotherapy at each recurrence appears justified by the success attending its use in the first attack. Under these circumstances, however, repetition of chemotherapy fails to prevent progressive tissue changes, fosters the development of resistant strain of micro-organisms, and may sensitize the patient to the drug. In the latter event the drug is then disqualified for the treatment of a subsequent and perhaps more serious infection.

During the *period of operation* antibiotics, used locally or systemically, appear to have considerable prophylactic value by preventing meningitis, controlling bacteriemia and protecting uninfected tissues in the operative wound from contamination.

In the *postoperative period* antibiotics limit the spread of infection to freshly exposed tissues and in most instances shorten the healing period.

Meningitis almost invariably follows *fractures of the paranasal sinuses* with a tear of the overlying dura. This complication can now be avoided by the prompt administration of the antibiotics and prompt surgical repair of the dura. When meningitis has already followed a fracture through the sinus wall with tearing of the dura, antibiotic therapy permits repair of the dural defect to be carried out after recovery from meningitis. Under these circumstances better clinical results are obtained by awaiting recovery from meningitis before proceeding with dural repair. Under continuing antibiotic therapy, fractures of the paranasal sinuses heal by primary union. Bone fragments, surrounded in part or entirely by viable soft tissues, exhibit amazing viability. However, bone fragments lying free within the sinus cavities require eventual removal. Sequestrum formation has been greatly minimized by antibiotic therapy.

The generally accepted rule that as little surgical intervention as possible should be employed in *acute sinus infections* has become even more rigid since the introduction of chemotherapy. Exceptions to this rule have been conceded in the presence of orbital extension, bacteriemia and retrograde thrombophlebitis, but the therapeutic use of the antibiotics has almost eliminated these exceptions, because penicillin rapidly controls orbital cellulitis of sinus origin, clears the blood stream of viable organisms and impedes the progress of intravenous infection. More than ever before should acute sinus infections be permitted to become chronic before deciding upon surgical intervention. In many instances the antibiotics eradicate the infection before a chronic process can develop.

Antibiotic therapy in acute sinus infections must be confined to those induced by micro-organisms sensitive to the drug and it has become obvious that sensitivity tests should be carried out if possible prior to administration of the drug. Treatment of acute sinus infections due to resistant strains of micro-organisms fails to prevent progression to a chronic status and the eventual need for surgery. Prolonged therapy with a single drug may render the strain resistant, thus making it possible for infection to affect a previously uninvolved sinus during the course of antibiotic therapy.

Chronic sinus infections are resistant to antibiotic therapy because the drug penetrates with difficulty the abnormal tissues resulting from repeated or prolonged infection. Tyrothricin lacks the ability to penetrate tissue, and its limitation to surface use renders its value in chronic sinus infections questionable. Even though penicillin and streptomycin temporarily control the infection, recurrence often follows soon after antibiotic therapy is discontinued and ultimate surgical drainage is required. When surgery alone is unsuccessful in eradicating chronic infection in the sinuses, antibiotic therapy is sometimes capable of playing a decisive rôle. The combined local and intramuscular use of penicillin after surgi-

cal failure brings about the disappearance of exudate and of viable micro-organisms. In most instances of chronic sinus infection in which irreversible tissue changes are extreme, a successful result can be obtained only by the combined use of surgery and chemotherapy.

In *meningitis*, the ears and the paranasal sinuses are the most frequent primary foci. In the past, surgical drainage of the primary focus has been axiomatic in the treatment of meningitis. In most instances an initial attack of meningitis may now be controlled by antibiotic therapy with or without surgical drainage of the primary focus. This has led many clinicians to doubt the value of drainage of the primary focus when chemotherapy is available. At least it has become apparent that surgery can be safely delayed until the meningitis is under control. When surgical drainage of the primary focus is then attempted, precision laboratory and roentgenological studies have been completed and the patient has become a better surgical risk.

Relapsing cases of meningitis occur with more frequency in sinus infections than in mastoid infections. Even though operation may be of little value in the acute phase of meningitis, it continues to deserve consideration in the treatment of a relapsing case. It must be conceded that the full recovery of many relapsing cases can be attained with chemotherapy alone but the fact that the chronic focus consists of a formidable collection of pus, and perhaps sequestra, as well, cannot be completely disregarded. Eventually such a focus must be dealt with surgically, and especially when reinfection of the meninges coincides with discontinuation of the chemotherapy. Attempts to prevent relapse by surgical attack upon an extradural source of infection have frequently been disappointing. Such failures seem more likely to be due to incomplete surgical drainage of a single focus or the presence of multiple foci which escape recognition. In the presence of an extensive focus surgical intervention cannot as yet be discarded in favor of chemotherapy alone. The concurrent use of chemotherapy and surgical drainage appears to be the best policy at the present stage of development.

Frank *osteitis* accompanying acute sinus infections has been generally controlled promptly by adequate doses of penicillin. Unfortunately, reactivation of the infection may appear upon withdrawal of penicillin and extension to the meninges follows. When systemic penicillin is again administered, the effective control of the meningeal infection permits delay in operation. In fact surgical intervention appears to be most effective if postponed until the meningitis is controlled.

Penicillin rarely effects a cure in osteomyelitis of the frontal bone with or without brain abscess. Surgical intervention with maintenance of adequate drainage is imperative. The concurrent administration of intrathecal as well as intramuscular penicillin, however, has effected some remarkable recoveries. In spite of antibiotic therapy all necrotic bone must be removed before healing can occur. While the antibiotics exhibit a peculiar ability to relieve the pain associated with osteomyelitis, their main value lies in their ability to prevent sequestration and arrest progressive extension of the infection. In osteomyelitis secondary to sinus infection, the antibiotics seem capable of reducing the extent of radical surgery upon the skull to a remarkable degree.

EXTERNAL SINUS SURGERY

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A REALISTIC approach to the problem of external sinus surgery is a prime requisite in any symposium on sinusitis. There are two reasons for this: the fear of the average layman engendered by advice for any sinus surgery, especially by the external route; and the necessity for the rhinologist to evaluate clearly just what he is offering the patient.

There is no question but that with modern chemotherapy many sinus operations—both intranasal and external—will be avoided. Yet in the presence of convincing evidence of necessity for an unavoidable external operation, the rhinological surgeon must not only know certain common techniques thoroughly, but also be able to evaluate them carefully before doing them.

In recently discussing the problem of external sinus surgery with a young well trained rhinologist who had graduated from one of the best otolaryngological hospital services about ten years ago, certain points of importance developed.

1. Although this doctor had had adequate training in both external ethmoidal and external frontal technique, he felt far more confident of the excellence of his work in the former.

2. He had recently been compelled to do a Lynch frontal because of an orbital abscess which had failed to improve with chemotherapy. At operation he had done a complete ethmoidectomy and had drained a large frontal space which he had supposed to be the frontal sinus, but which later turned out to be a very large frontoethmoidal cell. The frontal sinus itself was not entered at all. (But the very thorough ethmoidectomy was followed by uneventful "cure" of the patient!).

3. In several years' army service in the recent war this same doctor had seen a number of cases in which simple trephination of the frontal sinus had been done by civilian doctors *through the anterior diploetic wall!*

4. This led him to assume that many civilian specialists not only rarely do external surgery of the frontal sinus, but that some rhinologists may not be too familiar with present day external techniques.

During the war the writer acted as consultant and assistant to a young rhinologist at a Lynch frontal operation and found it necessary to lend him technical aid. It was pointed out that the operator had opened a large frontoethmoid cell which he had assumed was the frontal sinus; that there was inadequate exposure of the frontoethmoidal bony structure because of attempting to do the frontal sinus work first, independently of the ethmoid; that good exposure of the medial orbital wall was best obtained by detaching the medial palpebral ligament and elevating the periosteum; that in the Lynch frontal the easiest way into the frontal sinus is from the ethmoid by removing the lacrimal bone, and following the lacrimal and adjacent anterior ethmoid cells upward into the floor of the frontal sinus; that by having the patient sitting in a chair instead of lying on an operating table, he had in some respects made his task harder; etc.

In teaching internes external sinus surgery, some of our more mature staff members have indicated their desire to review their technical skill. It may be desirable therefore to recapitulate briefly some of the surgical techniques used in external surgery of the sinuses.

THE FRONTAL SINUS

A. The Lynch operation. Every rhinologist is familiar with the Lynch type of frontal operation. In the 15 years between 1930–1944 at the Massachusetts Eye and Ear Infirmary this was done 192 times in 447 frontal sinus operations on 276 patients (6). Therefore, in our hospital, it is the commonest operation on the frontal sinus, with obliteration running second with 123 cases.

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Lynch's original method (4) should be reviewed by all surgeons who may find it necessary to do the operation. He recommended complete exenteration of the ethmoid with complete removal of the floor of the frontal, of the ascending process of the superior maxilla, and posterior part of nasal bone.

My own technique is about as follows:

First, the patient's sinus roentgenograms are studied carefully.

With the patient lying flat on his back under intratracheal anesthesia, and with a well-fitting postnasal plug in the nasopharynx secured through the mouth, the skin of the face and nasal vestibules is sterilized, sterile vaseline or sterile boric ointment is applied to the conjunctival sacs, and the lids are sutured together on the side to be operated upon; this stitch is removed at the end of the operation. A vertical slightly curved incision is made with anterior convexity about halfway between the inner canthus and the midline, but slightly nearer the former than the latter; the aim is to make the final exposure quite near to the tear sac. The lower pole of the incision is slightly above the plane of the infraorbital margin. The incision is continued upward to curve outward, parallel to the inferior margin of the unshaven eyebrow, or into the crosshatched eyebrow itself. After a scratch outline of the exposure desired has been made, the incision is carried through the periosteum without bevelling the skin or underlying tissues. Bleeding vessels are clamped but not tied. The periosteum is then elevated, with detachment of the medial palpebral ligament, and of the pulley of the superior oblique, but with identification and preservation of the anterior ethmoidal artery and the nasociliary nerve. The artery provides exact orientation as to the level of the orbital plate of the frontal bone, and the cribriform plate, since it grooves the former inferiorly and lies upon the latter superiorly.

A Citelli or small Kerrison punch is employed to plunge through the lacrimal bone into the anterior ethmoid, which is followed upward to the floor of the frontal. The ethmoid cells are exenterated, temporarily leaving the capsule of the ethmoid except laterally; the anterior half or almost the entire lateral ethmoidal wall may be removed. Early in the exenteration of the ethmoid cells one may excise the anterior tip of the middle turbinate, followed by pushing a curette upward and outward to the lower level of the orbit, purely for orientation. In removing the lacrimal cell, care is taken not to injure the nasolacrimal duct. By preserving the medial wall of the ethmoid capsule temporarily, trauma to the septal mucosa is avoided; this is of great importance.

The floor of the frontal sinus is then removed completely. In the process, the upper end of the ascending process and as much of this process itself as possible is preserved, and so is the entire nasal bone. The frontal sinus lining is removed with care not to perforate the interfrontal septum.

Any frontoethmoidal cell present is removed along with whatever ethmoidal prolongations over the orbit there may be.

The medial wall of the ethmoidal capsule is removed. It is better to remove the entire middle turbinate but there is no especial point in removing the superior or supreme turbinates; their preservation aids in retention of the sense of smell, and avoids opening dural prolongations on the olfactory nerves.

The dissection of the medial ethmoidal wall is carried high anteriorly to within a few millimeters of the cribriform plate. This structure is identified exactly by very gentle palpation with a thin, blunt-edged septal dissector rather than a blunt probe, although the latter may be used if desired. The nasal septal mucosa must be preserved intact and uninjured throughout. No portion of the floor of the frontal should be allowed to remain in the ordinary Lynch frontal.

The foregoing procedures produce a field resembling a figure of 8, with one circle of the 8 represented by the frontal sinus, and the other by the exenterated ethmoid. The constriction between the two corresponds to the nasofrontal opening. It is closure of this opening which is one of the major causes for failure of the operation in certain cases. In closing the external wound, therefore, some surgeons place a drain or obturator between the frontal sinus and the nasal cavity, realizing that the anatomical hour-glass constric-

tion is actually much smaller than it seems when the open wound is inspected and then closed. This is because the anterior ethmoid is only about 5 millimeters in thickness from side to side, while only 3 millimeters more are gained from the coronal space at the relationship of the nasal cavity to the frontal sinus floor. The anteroposterior diameter of the frontal is important, in that the deeper the frontal sinus is from before backward, the greater is the ethmoidal relationship. The ethmoid widens gradually posteriorly to about 15 millimeters at the face of the sphenoid. It is to be recalled that the anterior boundary of the ethmoid is the posterior border of the ascending process of the superior maxilla, making the frontoethmoidal relationship a relatively posterior one. That is, the nasal bone and ascending process have a considerable anterior relationship to the nasal part of the frontal bone, and assure the frontoethmoidal surgical anatomy just described. The frontal ostium lies posteromedially in the floor of the frontal, very close to the region of the foramen cecum and erista galli.

Methods of keeping the surgical nasofrontal communication patent are still in the trial and error stage. Some of the methods are:

1. Sole reliance upon favorable anatomical factors and the control of infection with chemotherapy.

2. Tubes. Lynch himself left in a soft rubber drainage tube three-eighths of an inch in diameter with one end cut on a long bevel. He removed the tube after 5 days. The fenestrated bell-end of a large French soft rubber catheter may be left in frontal sinus with the small cut end secured just outside the nasal vestibule. This is an "irritating" foreign body, yet it has the advantage of being easily obtained, easily sterilizable, self-retaining, well-fitting, quickly and easily removable, and available for irrigation of the frontal sinus with chemotherapeutic agents if desired.

3. Mucosal flaps and skin grafts have been tried and at times found of value. The writer never uses the latter.

4. Probing is not of great value.

5. Nonirritating foreign bodies such as a tantalum tube, or tantalum foil secured on a soft rubber catheter with tantalum wire ties, tantalum foil in the Goodale operation, methyl methacrylate, etc., have been tried, especially in the secondary revisions of the Lynch operation.

If there is any question as to the need for free "wide and open" drainage, the wound is left open with adequate Miller rubber dam tubing appropriately secured to prevent closure. Otherwise the wound is closed with plastic suture material, and the sutures are removed about the third day post-operative.

B. Secondary Lynch-type frontal surgery. In 15 years (1930–44) experience of the surgeons of the Massachusetts Eye and Ear Infirmary there were 29 nonosteomyelitis cases who each had two to nine Lynch or Lynch-type operations and revisions—totalling 77 in number for the group. In the case having the highest number, it was possible to establish a nasofrontal opening 3 by 8 millimeters with "cure" during a follow-up of over 2 years.

These cases constitute a very difficult group and their management requires a thorough understanding of applied surgical anatomy, and of fundamental healing processes of bone, connective tissue, and epithelium in the frontal region.

The causes of failure in the Lynch operation have been listed (3, 6) as (a) residual frontoethmoidal cells and undrained orbital prolongations of ethmoidal cells; (b) remnants of the frontal floor; (c) adhesions; and (d) bony occlusion of the nasofrontal opening. In well performed operations, the cause of greatest importance is simple closure of the nasofrontal opening. The writer believes that (b) is not usually due to inadequate removal of the frontal floor, but more often to simple regeneration of bone (6).

In Lynch-type "revisions" the above mentioned factors are dealt with as effectively as possible. An effort is made to re-establish nasofrontal drainage; the particular method chosen must be determined by the circumstances of the individual problem. The choice of an obturator-drain usually lies between a soft rubber French catheter and some form of nonirritating foreign body, such as tantalum, acrylic resin, fibrin film, etc.; *any* foreign body must be well fitting. If the rubber catheter method is used, it should be left

for a very few days or for many weeks, and heavy dosage with penicillin used for the control of infection.

The cleaner the healing field (less infection) the better. It is the infection factor which is a major cause for the proliferation of granulations (inflammatory and osteoid) and the inhibition of epithelial growth. The opposite process is required in surgical healing.

THE CONTRACTURE PROBLEM

Early and late contracture are probably important in causing closure of the nasofrontal opening in both primary and secondary Lynch-type operations. Late contracture is caused by shrinkage of collagen fibrils; the less the granulation tissue and the quicker epithelization occurs in the region of the surgical nasofrontal communication the less likely is such contracture to be a factor. Early contracture begins after about 2 to 5 days, progresses rapidly for several days, and then gradually subsides. It is *early* contracture which obturator-drains are supposed to lessen, since such devices are removed in from 2 days to about 2½ weeks (1) by the majority of surgeons.

Anthony feels that such a device should be left beyond the secondary contracture phase of healing. The writer has a case with a permanently implanted tantalum tube in an unobliterated frontal sinus for over 2 years with no recurrence of trouble. A tantalum covered nasofrontal catheter left 4½ months in a tuberculous rhinitis case complicated by frontoethmoidal sinusitis and orbital abscess failed to establish satisfactory drainage, and further surgery was required.

Primary or secondary contracture may be lessened by attention to the following; granulation tissue surrounded by a circle of bone tends to contract toward the periphery of such a circle (Kazanjian) whereas granulation tissue surrounded by soft tissue only tends to contract centrally. The more nearly a nasofrontal opening in the Lynch procedure has a bony circumference, the more likely it is to stay open. This merely means that so far as is consistent with thorough and adequate technique, the upper end of the ascending process and the nasal bone should be preserved.

In summary, secondary revisions of Lynch frontals without obliteration require a certain amount of ingenuity, a fundamental knowledge of surgical anatomy, and of the surgical healing of connective tissue, bone, and epithelium, if obliteration is to be avoided.

C. Obliteration. Failure of the Lynch or Lynch-type revision causes many experienced rhinological surgeons to consider obliteration as a solution to the problem. This means the collapse of the soft tissues of the anterior wall against the bony posterior wall or dura so that (a) no air space or gross mucoperiosteum remains in the sinus, and (b) the frontal ostium is sealed off by scar tissue, with the result that (c) obliteration of the sinus results, together with (d) deformity, relatively slight with a "shallow" frontal, and severe with a large "deep" sinus. Sometimes obliteration is undertaken as an original procedure; .e.g., in the Mosher technique for excision of an osteomyelitic frontal squama, both sinuses were usually obliterated with removal of all walls. (The writer has not been compelled to remove the frontal squama in osteomyelitis since the release of penicillin for general use, but has had to obliterate the frontal sinuses in osteomyelitis limited to the sinus area.)

In every obliteration the anterior wall is removed from the frontal sinus. In addition, the floor may be removed or partly removed; the posterior wall may be removed; and in bilateral obliterations the interfrontal septum is removed. Mosher believes removal of the anterior and posterior walls and a little of the floor is most likely to succeed.

In obliteration, it is desired to *seal off* any communication between the frontal sinus and the nasal cavity; if this is not an easy problem, obliteration may not be necessary. In contrast, the Lynch-type of procedure makes every effort to establish a nasofrontal communication surgically. It is surprising that in Lynch or Killian operations, postoperative mucoceles (or pyoceles) were found to be commoner (13 cases) than after obliteration (3 cases) in a review of 276 external frontals at the Massachusetts Eye and Ear Infirmary between 1930–44. Such mucoceles or pyoceles are, in my opinion, due to absence of nasofrontal drainage with secreting mucoperios-

teum in the frontal area which produces a cyst.

In 77 obliterative cases having osteomyelitis at the Massachusetts Eye and Ear Infirmary, 25 required further surgery. In 46 others having no osteomyelitis, 8 required additional operations directly upon the frontal sinus. This equals about 27 per cent failure for this type of procedure, as compared with 34.5 per cent for the entire group reviewed by the author in which *all* frontal operations of all types are included.

Incidentally, 71 of 123 obliterative cases required about 1.5 plastic procedures each for the repair of deformity, with an average of about 1 year's time for such work. The longest time was just over 5 years for 3 plastic operations in one of the cases.

D. Simple trephination of the *floor* of the frontal sinus with establishment of external drainage is useful in combination with chemotherapy in dealing with certain fulminating acute infections occasionally encountered. The frontal floor has no diploe except near its anterior and external margins, and the trephine opening is made without disturbing this diploe. The frontal sinus lining is removed only at the point where the drainage tube is placed. Local and systemic penicillin therapy are carried out; when the penicillin can be freely irrigated from the drainage tube into the nasal cavity, and external drainage ceases, the tube is withdrawn.

After patient has recovered completely, he should have his nasal cavities made as mechanically and physiologically perfect as possible and further external surgery avoided if possible.

MacKenzie Brown (6) has reported treating certain chronic frontal sinus cases by simple trephination also.

E. The Jesberg and Lothrop operations are not commonly used in our hospital and will be omitted from this discussion.

THE ETHMOID AND SPHENOID SINUSES

External surgery of the ethmoid is no different technically from that of the Lynch frontal except that the frontal area is left undisturbed and the problem of making a nasofrontal communication surgically is thereby deleted. In both the Lynch frontal and the external ethmoid operations the sphenoid may be opened and explored from its ethmoidal relationship if desired.

THE MOURE OPERATION

The Moure operation for excision of malignant tumors of the sinuses is a formidable undertaking. Its risks may be lessened by the following considerations:

1. Anesthesia is best given intratracheally with a balloon corking the glottis. Since oxygen is easily exploded by a diathermy apparatus, its use must be avoided. That is, air-ether mixtures are employed, not oxygen-ether. This is accomplished by discarding the usual ether machine, and substituting a large ether can which has several large holes made into its top, each hole being about the size of a dime. The intratracheal tube is attached to the mouth of the ether can, and the patient's normal respiration sucks in air over the ether in the can, with enough ether vapor to maintain surgical anesthesia. While the ether can be exploded by the diathermy apparatus, this risk is relatively slight with careful use of the machine. Both the nasopharynx and hypopharynx are packed with postnasal plugs secured externally through the mouth.

2. Both plasma and saline for intravenous use should be set up in the operating room, and administered alternately throughout the operation. The anesthetist can most conveniently do this. Arrangements for transfusion, to be done if necessary, should be made prior to operation.

3. A highly efficient coagulation and cutting diathermy apparatus should be part of the equipment utilized. The writer prefers the large Davis-Bovie machine.

4. The Moure incision is improved cosmetically and for practical exposure of the underlying field by making it slightly S-shaped. Its upper end starts at the lower aspect of the inner margin of the eyebrow, and proceeds downward anterior to the tear sac region, then near the posterior margin of the lateral nasal surface to the posterior aspect of the ala nasi. *It continues onward* until the posterior margin of the ala nasi has been cut through and the nasal vestibule freed posteriorly almost to its medial aspect, the incision ending near the nasal columna posteriorly, but

not involving the upper lip directly or opening into the vestibule. It is this last portion of the incision which allows very free mobilization of the soft tissues of the cheek to expose the pyriform aperture and upper jaw anteriorly. It will almost always avoid the necessity for making a transverse incision in the cheek. Bleeding is carefully controlled.

A line of cleavage around the pathological mass can usually be found by blunt dissection and this, plus diathermy cutting and coagulation, will greatly limit blood loss. After getting the mass as widely dissected and freely mobilized as possible, it is very quickly excised without regard to hermorrhage for the two or three minutes required for gross removal with the largest usable destructive instruments. Then hemorrhage is again quickly controlled, and the removal continued until the tumor has been grossly excised and all suspicious areas coagulated with surgical diathermy. Adequate drainage into the nose is obtained if this has not already been accomplished by the excision of the mass. The wound is closed with plastic sutures without drainage externally.

Any sinus, the nasal cavity, and nasopharynx can be reached as desired by this approach as described or slightly modified. If the hard palate and alveolus are involved with the antrum alone, it is possible easily to reach as high as the orbital floor through appropriate mouth incisions and excise the mass without any external incision.

With highly radiosensitive tumors the Moure operation need not be done, since the simple provision for sinus surgical drainage plus adequate irradiation will suffice. In any event, a radiosensitive sinus tumor should be adequately irradiated whether or not the Moure operation is done.

POSTOPERATIVE CARE IN EXTERNAL SINUS SURGERY

In the hospital period of convalescence, ordinary surgical principles are followed for supportive treatment, including chemotherapy as seems necessary. If the wound has been closed the sutures are removed about the third or fourth day if possible. If at operation the decision is made to leave the wound open because of the imperative need for control of sepsis, the surgeon *should be in no hurry to close it.* The patient's safety is of first importance. Incidentally, surprisingly good cosmetic results are common in wounds left open for considerable periods of time.

Mosher's dictum "once a sinus always a sinus" does not correspond to the writer's experience if adequate follow-up care is given the individual patient. Swimming and recurrent acute upper respiratory infections are common causes of acute exacerbations of sinusitis, which can be avoided or brought under control.

In polypoid sinusitis cases undue reliance is often placed upon the management of allergy. While every aid should be gratefully accepted, the polypoid degenerative tissues will nevertheless sometimes recur massively. This problem is, at the present time, best solved by the use of coagulation diathermy to destroy such tissue as it appears, or removing small such areas periodically.

SUMMARY

The technique of several external surgical operations useful in sinus surgery has been summarized, particularly the Lynch frontal operation; secondary revision of postoperative frontal sinuses by a Lynch-type procedure; obliteration of the frontal sinus; simple trephination of the frontal sinus; incidental techniques for the external ethmosphenoid approach; and the Moure operation. Some experience has been cited in evaluating these procedures. The Moure technique, for radical antrum surgery has been discussed.

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INTRANASAL SURGERY

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THE fundamental principle of intranasal surgery is the re-establishment of normal ventilation and drainage of the sinuses and when this can be accomplished by intranasal surgery, it is preferable to radical surgery.

ANESTHESIA

Local anesthesia is preferable for intranasal surgery. The patient should be buffered with a substantial dose of the barbiturates and a sedation dose of morphine. Whether atropine or scopolamine is used depends upon the operator's choice for the difference between the two is academic. A committee appointed by the American Medical Association reported in 1920 that they diligently studied the question of mixed local anesthetics and found that a single anesthetic was safer than combining a local as cocaine and infiltration, such as novocain. Ether is a poor anesthetic for intranasal surgery, but is safer for children than is any form of intravenous medication. Sodium pentothal combined with a local anesthetic is an ideal anesthesia for nervous patients.

SUBMUCOUS RESECTION

The correction of nasal obstruction constitutes more than 60 per cent of the intranasal surgery of today. Too often a rhinologist unconsciously asks himself during a nasal examination, "What do I see that I can correct?" His eye may discover a deflected septum or a hypertrophied turbinate and immediately that bit of pathology is considered the cause of the patient's complaint. Early obstructions tend to retard the pneumatization of the sinuses and the normal growth of the alae nasi and upper maxilla. The paranasal sinuses can pneumatize normally with a complete occlusion of the vestibules or the choanae; on the other hand an early septal deflection which jams the middle turbinate against the lateral nasal wall will obstruct the infundibulum, blocking the nasofrontal duct or the ostium of the antrum, thereby arresting pneumatization of the sinuses which have their origin from this region.

Deviated septa occur more frequently in civilized races than among savages. Schaeffer states: "The nasal septum . . . . . encroached upon more and more by the forward cranial extension incident to brain growth as one passes from the anthropoids to the ultra-civilized races of man."

Headaches which are caused by nasal obstruction vary from slight nasal discomfort to severe neuralgias. The simple thickening of the septum high between the middle turbinates will interfere with the normal physiologic swelling of these turbinates. These patients appreciate their obstruction when they remain out-of-doors during cold weather or during an acute cold. This type of case receives a good result from a well performed submucous resection.

There is a deformity caused by a backward development of the sphenoidal process of the septal cartilage on a spur of the vomer. This large spur crowds the posterior fourth of the middle turbinate and is capable of persistent trouble. Whenever the middle turbinate enlarges, contact will be made and pressure exerted directly upon Meckel's ganglion. This is very noticeable during the menstrual period. The growth of this spur interferes with the size and shape of the middle turbinate and by extending laterally will encroach upon the ostium of the antrum. This deformity favors maxillary sinusitis by blocking the ventilation and drainage of the antrum. "A good thinker needs a clear head." "A dull child of hypertrophied adenoid is but an exaggeration of the adult with a blocked nose." The inability to breathe through the nose slows the cerebration and clouds the memory. As expressed in the words of Shakespeare, "A man so dull, so dead in looks, so woe begone."

The method and degree of packing after a submucous resection has ranged from none

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through light, to metal clamps and tight packings capable of being kept moist. If there occurs a small perforation or tear, no precaution is necessary, but if there is a bilateral tear, whose edges are opposite, it is recommended that a piece of Cargile membrane be placed between the flaps to serve as an arbor and also a barrier to the formation of a permanent perforation.

ETHMOIDAL LABYRINTH

An anterior ethmoidal cell migrates into the frontal to pneumatize the frontal sinus. Inflammations, allergic reactions or chronic degenerations of the anterior ethmoidal cells will block the frontal duct producing frontal sinusitis. The inward displacement of the middle turbinate is the simplest procedure to improve the drainage of the frontal sinus. Probing and irrigation of the frontal sinus was once a major procedure, and before the days of good roentgenograms was hazardous and only attempted by the masters.

INTRANASAL FRONTAL OPERATION

The resection of the anterior end of the middle turbinate and the removal of hypertrophies and polypi of the middle meatus will give immediate drainage to a mildly blocked frontal sinus. If rupture of the sinus is eminent with a risk of an orbital cellulitis, an external trephination should be done for immediate drainage. When the frontal empyema is chronic, the hypertrophies about the nasal frontal duct must be removed to maintain drainage. The resection of the middle turbinate is performed by resecting its anterior attachment and the removal of the tip with a cold snare. If there is a high septal deflection, this must be resected to obtain sufficient operative space. The removal of the hypertrophied uncinate process and the adjacent ethmoid cells contribute to the exposure of the frontal duct. It is not considered good surgical practice to interfere with the lining of the duct for fear of future contractions. The postoperative treatment consists of irrigation of the sinus with antibiotic solutions. Many rhinologists initially irrigate with a peroxide solution as the offending bacteria are frequently anaerobic.

HALLE OPERATION

Halle's method depends upon the resection of a mucoperiosteal flap and the thorough removal of the agger nasi and sometimes a part of the process of the superior maxilla. The diseased anterior ethmoidal cells are thoroughly exenterated and the duct enlarged by burrowing, and a resection of the floor of the frontal sinus. The flap is tamponed into the outlet and allowed to heal. This operation cannot replace the radical operation of Lynch, when the lining of the frontal sinus is diseased, but if a radical must follow, the intranasal approach will be an added advantage.

Ingals designed a self-retaining gold cannula to keep the nasofrontal duct patent, and lately strips of tantalum have been advocated by Goodale to maintain the patency of the duct.

INTRANASAL OPERATION UPON THE ETHMOIDAL LABYRINTH

The appreciation that infections of the posterior ethmoidal cells and the sphenoid sinus were the causative factors in many of the optical nerve disorders prompted the perfection of operations designed at their exenteration. Mosher advocated removal of a portion of the middle turbinate to enter the ethmoidal labyrinth. The cells were curretted backward from above down passing from the anterior into the posterior group. This operation was the first of the American procedures to receive international recognization.

Ballenger's operation attempted to remove as much as possible of the ethmoidal labyrinth *en masse*. With a specially designed knife, the ethmoidal labyrinth was carved free around its posterior, superior, and anterior borders and the resected mass was drawn from the nose.

The sphenoethmoidal labyrinth is too delicate, and its relationship to the meninges is too close to sanction such a radical procedure *en masse*. Then, too, there are so few perfect labyrinths, and the anatomic variations are so great that the method is limited to only selected cases in the hands of a very few surgeons. Hajek resected the middle and superior turbinate with his hook and reduced the anterior wall of the sphenoid and the posterior ethmoidal cells with the same hook, by insert-

ing the hook posteriorly and drawing it forward, and removing the shreds with forceps. Sluder improved this technique by the use of his knife and removal of incised cells with a sharp biting forceps. Yankauer eliminated much of the bleeding by ligating the terminal branches of the sphenopalatine artery.

J. A. Pratt demonstrated that the exenteration could be accomplished without sacrificing the middle turbinate. When the middle turbinate and the ethmoidal cells were extensively removed the pathological process was eliminated but the ventilation of the nose was changed and the unrestricted air currents striking against the sphenoidal area frequently produced a hypertrophy of the anterior wall of the sphenoid sinus which obliterated it.

ANTRAL DRAINAGE

The resection of the nasoantral wall for drainage of the maxillary sinus is the simplest but frequently the best intranasal operation. The insertion of a hard rubber drain minimizes the size of the window and makes this operation acceptable for children. Robinson advocates compression of the antral membrane by a balloon for the cure of allergic sinusitis. Whether the anterior end of the inferior turbinate be amputated or displaced must vary according to the position of the floor of the naris with relation to that of the antrum or the degree of hypertrophy of the turbinates. The operation can be spoiled by insufficient drainage or excessive ventilation with a loss of the physiological function of the turbinate.

POSTOPERATIVE CARE

The immediate complication of intranasal surgery is hemorrhage, and the best method of its prevention is a well placed pack. The type of packing used should be impregnated with an oil, and if it is to remain in over 48 hours it should contain some form of antiseptic. The ideal packing is so placed that the free ends remain outside the vestibule and folded within the nose to form a sac that cannot slip down into the nasopharynx.

If there has been free bleeding during the operation the terminal branches of the internal maxillary artery can either be coagulated or clamped off with small silver dural clips. The center of the pack may be a cotton roll or splint capable of being saturated with a vasoconstrictor. If oozing continues after 30 minutes or begins freely after an hour, it can be controlled by the administration of 5 minims of surgical pituitrin given hypodermatically every 15 minutes for 3 doses. Surgical pituitrin is also of value when administered before and after the nose is unpacked. Fortunately, infections seldom complicate intranasal surgery, but when they do occur must receive careful attention. Late secondary hemorrhage results from the separation of scabs and should be handled by the thorough cleansing of the nose of all clots; the control of the bleeding by adrenalin packs and the cauterization of the bleeding granulations. The use of oxycel, an absorbable oxidized cellulose, as an intranasal packing has the advantage of not requiring removal and is recommended for the invisible hemorrhage especially those from beneath the inferior turbinate.

CONCLUSIONS

The fundamental principle of intranasal surgery is the re-establishment of normal ventilation and drainage of the sinuses and when this can be accomplished by intranasal surgery, it is preferable to radical surgery.

The generation of surgeons trained in intranasal surgery is fast fading and the number of these operations has been reduced by a better knowledge of the physiology of the nose and the therapy of antibiotics.

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THE CLOSURE OF SURFACE DEFECTS WITH FREE SKIN GRAFTS AND WITH PEDICLE FLAPS

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IN the Medical Department report of World War I, about 300 pages are devoted to plastic surgery; no mention is made of free skin grafting, however, except that in one sentence a graft inside the mouth is suggested. Also no mention is made of the treatment of burns. In contrast to this, in World War II roughly one-third of the work in the centers for plastic surgery was the treating of wounds by free skin grafting and in addition a large volume of work was done in treating burn defects.

After World War I, plastic surgeons in civilian practice developed methods and services for the repair of extensive burns, and, except for a short time during which excessive attention was focused on the irreversible sealing methods of treatment (tanning), steady progress has been made in a basic philosophy of treatment of deep burns, viz.: to make open areas as clean as possible as soon as possible and to restore skin that has been lost. Still further progress has been made in the concepts of treatment that aim at the start toward keeping burned areas clean. However, the essential point remains that deep burns are apt to become infected and certainly in military surgery they cannot all be kept ideally clean. There have been cared for in the plastic centers patients by the hundreds with no skin on their heads, faces, or hands, and with large open areas over the body and extremities, with sloughs, contamination, infection, pain, and when evacuation has been delayed, with the usual "blown" contamination that results from lack of change of dressing.

These patients present all the problems of nutrition, chronic shock, blood chemistry, and wound healing that may occur, and these complications are all dependent on open wounds. Therefore, the basic surgical consideration is to get the wounds healed as soon as possible, by means of free skin grafts. Any spontaneous healing that may occur is welcome, but long delay in waiting for spontaneous healing, adds pain, contractures, and fixation of joints, as well as a chance for further depletion. As large open wounds heal either spontaneously or by grafting, the general condition improves proportionately. In some instances grafting has been done in spite of the presence of local infection uncontrolled by chemotherapy; such a graft to close the wounds has been life-saving. Raw open areas as large as 200 square inches are frequently successfully grafted at one operation. These extensive procedures as well as others for the restoration of function, in the words of one World War I surgeon, "would have been fantastic" at that time.

While free grafts have been used most extensively in repairing burns, they have been applicable and valuable also to cover large open areas for other causes, such as gunshot and shell fragment wounds. One of the most important areas to benefit from free grafting is the hands. By early closure of burns and other defects of the hands, there have occurred many dramatic results in which function that otherwise would have been lost has been preserved. This statement applies to other ex-

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Fig. 1. Widespread burn restored in minimum number of operations with split skin grafts.

Fig. 2. Complete crippling of hand restored in a single operation of free skin grafts.

Fig. 3. Widespread loss from shell fragment. Restoration in one single operation with free skin grafts.

Fig. 4. Chronic traumatic ulceration of both legs. Disabled many years. Complete healing following single operation with free skin grafts.

Fig. 5. Restoration of eyelids with full thickness grafts from clavicular region.

tremities. In some plastic centers, most of the work has been on the hands and extremities and only about one-third of the work has been on the face.

For making very extensive repairs, the split skin graft, or some version of it, must be used so that the donor site will heal promptly. In cases in which 250 square inches are transferred at one time, it is essential that a method of grafting be used in which prompt healing of the donor site can be had. If grafts are cut too deep, much added crippling may occur. In some instances it has been necessary to discharge patients because of trouble in donor sites that exceeded the original lesion.

A special area about the face may be mentioned and that is the eyelids. When eyelids are burned and contractures follow, the eyeball is left exposed and impairment of vision may result. In hundreds of instances satisfactory protection of the eyeball by the lid has been regained with a free skin graft to resurface the lids. A special type of graft has been used for this work that is adaptable in function as well as color and appearance. Such a graft is of full thickness and is taken from the clavicular region; the supply is limited, but it affords the best color match and because of its character, presumably from its position in the platysmal area, gives excellent function.

Homografts have been used frequently to tide seriously ill patients over critical periods. These grafts, of course, are not permanent, usually lasting from 3 to 12 weeks. The wounds are literally "dressed" in the homografts. These grafts can be taken at autopsy if complete releases for the procedure can be obtained from the relatives and the patient. Such grafts have been taken as long as 4 hours after death and have been stored "refrigerated" for 6 more hours so that successful homografts have been done after as much as 10 hours' delay. Longer periods have been recorded but the use of refrigerated skin has not been developed into a routine procedure.

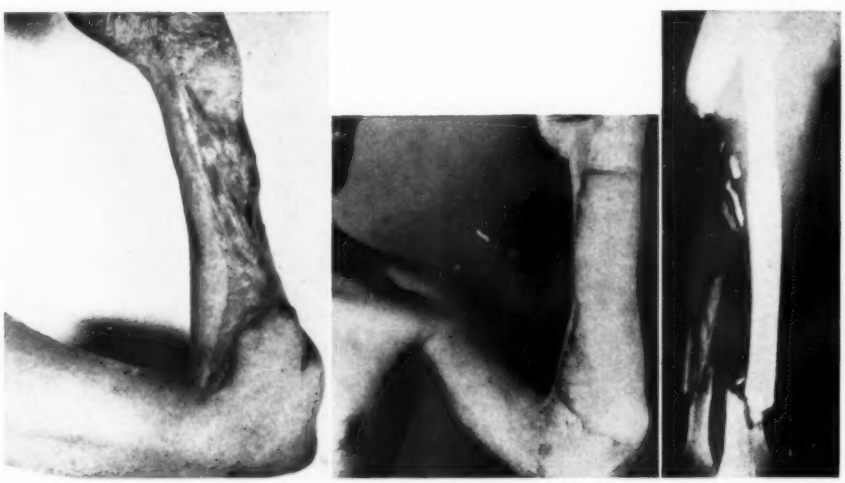

Fig. 6. Direct flap restoration of full length of forearm; 18 days' fixation to the abdomen.

In the use of free skin grafts (as in other procedures in plastic surgery) a tendency has been noted to suppose on one hand that perfection can be obtained in difficult restoration of features and surface smoothness and on the other hand to neglect simple procedures in grafting that could result in healing of long-standing lesions or deformities. For example one soldier was seen who had been off duty practically all of 9 years with traumatic ulcers of both legs. These were grafted in one operation and the patient was sent to duty.

In lesions for which free grafts will not suffice, such as gunshot and shell fragment wounds, and in cases in which features are lost, restorations with pedicle flaps must be done. Whereas in the past the majority of flap repairs have been done with tubed flaps, it has been demonstrated in hundreds of patients that direct (or delayed) flat flaps can be used successfully. The principle of a short broad pedicle is substituted for that of a long narrow tubed one, and if the application can be made as a direct transfer (that is without delaying the flap) a procedure may be completed in days that otherwise might require months. This has accounted for the saving of thousands of patient hospital months.

One of the main usages for the direct flap is in the repair of hand and arm defects. The flaps can be put on at early dates following the injuries, or later after the extremity has healed. It is possible to cover practically a whole forearm with a direct flap from the abdomen in 18 to 20 days, and many seriously damaged extremities have been saved. It might be said that these procedures are the opposite of amputation. When applied early, union of underlying fractures has been found to progress more rapidly and successfully and function is necessarily established at the earliest date.

In late deformities with surface scarring and with defects of nerves, tendons, bones and joints, it is essential to obtain adequate surface "healing" with a flap before satisfactory deep restorations can be done. The deep healing can be no better than the surface healing, and patients have been seen with wire, foil, screws, plates, bone grafts and bone fragments protruding through wounds that did not have adequate surface healing. By removing dead and foreign material, dissecting scar back to an adequate minute blood supply, and naking a repair with a flap of suitable thickness, so that the deeper tissues can be approached through good viable tissue that will heal promptly and protect whatever repair has been carried out on nerve, tendon, bone or joint, the orthopedic or neurological surgeon has been afforded valuable assistance in his work.

There are details and variations of work too burdensome for this report, but it is of importance to call attention to the fact that thousands of wounded soldiers have been successfully restored from serious surface defects by direct methods of free grafting and flap transfers.

The work has been done by many different civilian surgeons working in the services and in amount far in excess of any other period. Amputations have been practically nil as has also the operative death rate. Good teamwork is necessary between surgeons, nurses, anesthetists, rehabilitation workers and, of most importance, the wounded patient.

NEUTRALIZATION OF COLOR IN CAPILLARY HEMANGIOMAS OF THE FACE BY INTRADERMAL INJECTION (TATTOOING) OF PERMANENT PIGMENTS

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IN the treatment of capillary hemangiomas of the face the goal is the obliteration of the lesion so that appearance approximates normal. The authors' observations to date have led to the opinion that current methods of treatment including electrodesiccation, cauterization, radiation, sclerosing agents, and carbon dioxide snow are not satisfactory. Moreover, the plastic excision of such lesions from the face leaves much to be desired since usually it is necessary to resort to the use of a free graft of skin. Small grafts of skin taken from the postauricular area or from the supraclavicular area match the color of the skin of the face very well but if a larger graft is used this must be taken from a protected surface of the body the color match of which is not acceptable. Often such skin grafts on the face must be treated by the permanent injection of insoluble pigment (tattooing) into the derma in order to effect improvement in appearance. Therefore, the possibility of injecting pigments into the skin overlying capillary hemangiomas has been suggested. Results following permanent pigment injection of 7 cases of capillary hemangioma on the face are reported herein.

The process of tattooing for religious, ornamental or identification purposes is reported as far back as 2000 B.C. in Egypt and 1100 B.C. in China. Today mankind continues to practice tattooing for these same reasons. Natives of the jungles still use this practice as a method of tribal identification and civilized peoples still employ tattooing for physical decoration. The use of tattooing as a form of medical therapy can be traced to 1835 when Pauli employed it in the treatment of nevi, "congenital purple placques" and other lesions of the skin. Cordier (1848) advocated the tattoo treatment of nevi, and Schuh (1858) had the idea of using skin previously tattooed and then transplanted to the site of repair in the practice of cheiloplasty. In 1879 de Wecker used India ink successfully in coloring the corneal parenchyma. Thirty-two years later (1911), Kolle reported the use of tattooing with rose pigment to change the contour of the vermilion border of the lip. He also pointed out that nonadherent, flat, white scars were improved in appearance by the use of tattooing. Knapp (1925), and Duggan and Nanavati (1936) used gold and platinum chloride to tattoo scars of the cornea. Pickerel (1946) has demonstrated evidence in color photographs of excellent results following the tattooing of the cornea. Credit is given to Morestin, to Mauclaire, to Dufourmentel and to Passot by Bankoff (1943) for introducing the treatment to general plastic surgery. In the recent literature, Hance, Brown, Byars and McDowell (1944) called attention to the value of tattooing in the color matching of skin grafts and flaps on the face and in the simulation of the vermilion of the lip. Byars (1945) also reported successful intradermal pigment injection for color matching purposes in 60 cases of free skin grafts and flaps of tissue on the face. Brown, Cannon and McDowell (1946) reported improvement in appearance of one patient with a capillary hemangioma of the face following permanent injection of tattoo white and Chinese white.

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TECHNIQUE

The area to be injected is washed with soap and water, painted with aqueous solution of merthiolate and draped with sterile towels. Instruments and pigments are sterilized. The

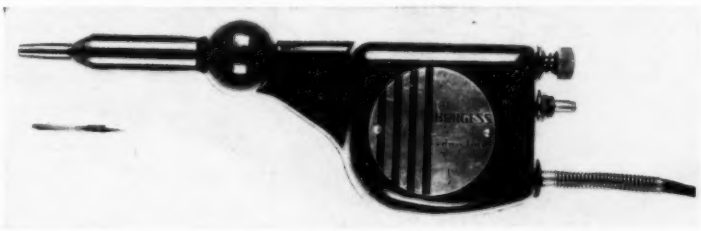

Fig. 1. Electromagnetic device with six needles which is used in the permanent pigment injection of capillary hemangiomas.

echnician wears sterile rubber gloves. The rea should be free from infection. It has been ound expedient to use the standard electro- nagnetic device to which six needles are at- ached. This is shown in Figure 1. With terile water the pigments are mixed into a hick paste which is picked up in the cup of he needle holder when the needles are with- drawn into its shaft. The current which auses rapid oscillation of the needles is oper- ated by a foot control. The needles are in- serted into the skin at an angle of approxi- mately 60 degrees so that the pigment will be injected obliquely at varying depths in the derma. In the tattooing of skin grafts bleeding from the needle holes is minimal. Bleeding may be bothersome when injecting capillary hemangiomas. The basic pigments which are in use at present include the following:

White	Titanium (or zinc oxide U.S.P.)
Yellow	Oxide of iron
Red	Mercury sulphide (or cinnabar)
Blue	Cobalt blue
Black	Black oxide of iron
Green	Hydrated chrome oxide

Combinations of these pigments usually will produce the desired tints. In addition ochre, sienna, and other earthy metallic oxides may be used. All of these pigments are insoluble and they may be sterilized in 70 per cent alcohol or may be autoclaved. The mixture of colors varies with the individual case. For the covering of capillary hemangiomas, white is the basic pigment, occasionally mixed with a very small amount of red or green. At the first treatment, a small area is injected and a record is kept of the color combination. Three

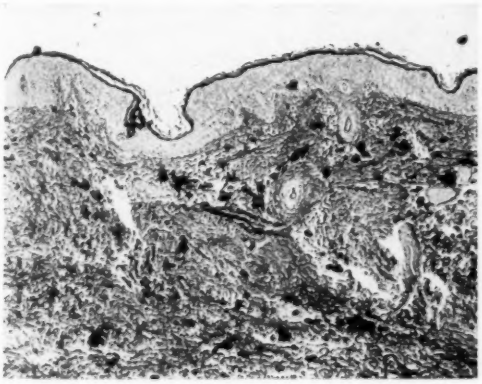

Fig. 2. Low power photomicrograph of capillary hemangioma after injection of pigment. Note that the particles of pigment are deposited chiefly in the upper layers of the derma, superficial to the capillary dilatations.

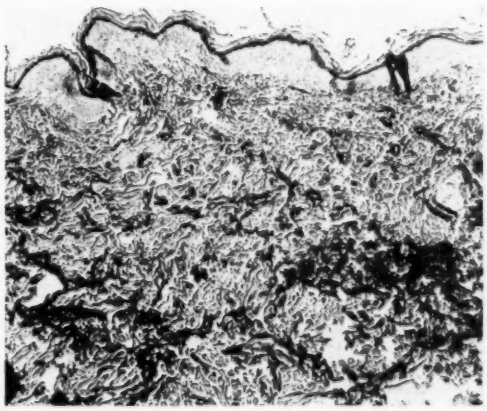

Fig. 3. Low power photomicrograph of normal skin tattooed for decorative purposes by a commercial artisan. In comparison with Figure 2 the pigment is more dense. It is scattered indiscriminately but is concentrated in the deeper layers of the corium.

TABLE I.—CAPILLARY HEMANGIOMAS TREATED BY TATTOOING

Case No.	Diagnosis	Size of lesion	Pigments used	No. treatments	Result
1	Capillary hemangioma (cheek)	6 x 5 cm.	White	3	Marked improvement
2	Capillary hemangioma (cheek)	5 x 5.2 cm.	White Green	2	Marked improvement; lesion barely perceptible
3	Capillary hemangioma (cheek)	8 x 2 cm.	White	5	Marked improvement; lesion barely perceptible
4	Capillary hemangioma (cheek and eyelids)	10 x 9 cm.	White Green Red	13	Result excellent
5	Capillary hemangioma (neck and cheek)	13 x 7 cm.	White Green	12	Marked improvement; some scarring of skin
6	Capillary hemangioma (cheek)	5 x 7 cm.	White	1	Marked improvement. Another treatment will be necessary over entire area
7	Capillary hemangioma (cheek)	10 x 9 cm.	White	4	Improvement; still under treatment. One-third of lesion has been injected

to four weeks are allowed to elapse before judgment is passed on the effect of treatment. Usually there is some absorption or desquamation of pigment and a second or a third treatment over the same area may be necessary before the desired result is obtained. Following the treatment a sterile dressing is applied. The patient is seen in 24 hours at which time a crust is present over the area which has been injected. As this peels away during the next 6 to 10 days the effect of the injection may be observed. Once the proper combination is decided upon, treatments may be given at 2 week intervals until the entire lesion is injected. An area of 2 to 3 square inches may be injected in a 1 hour sitting by a skilled technician. The number of treatments depends upon the size of the lesion. The injection causes some discomfort but the average individual tolerates this without anesthesia. In 1 case in the series, that of a child 3½ years old, the patient was admitted to the hospital and the treatment was given under avertin anesthesia.

OBSERVATION ON THE DEPOSITION OF PIGMENT

Figure 2 shows a low power microscopic section taken from a portion of a capillary hemangioma which had been tattooed (Case 1). The section shows a strip of skin with extensive tattooing and a rather fibrous corium. As noted in other examples, all colors of pigment appeared black, occasionally with a reddish brown tint, on microscopic examination. It is impossible to distinguish the different colors either in stained or unstained sections. The pigment is scattered mostly in phagocytes in the upper layers of the corium. This figure is in contrast to Figure 3 which shows a low power microscopic section of skin taken from an area tattooed on the arm for decorative purposes by a commercial artisan. Here the pigment is much more dense. It is scattered more indiscriminately but is chiefly in the deeper layers of the corium and is massed about the ducts of the sweat glands. Study of microscopic sections of capillary hemangiomas leads to an understanding of the mechanism of color in these vascular abnormalities. The melanin which gives color to the skin is in the stratum germinativum of the epidermis. The vascular channels of the capillary hemangioma are in the subcutaneous tissue and, to a lesser extent, in the deeper layers of the derma. The intensity of the red color of the great numbers of erythrocytes in the hemangioma reflected to the surface through the normal

Fig. 4. Case 4. a, Capillary hemangioma of cheek and eyelids. At the time of this photograph the lower portion of the lesion had been given 2 treatments of pigment injection. b, Result after patient had been given 13 treatments. There was moderate, transient edema of the eyelids following the injections of pigment into the skin of these areas.

Fig. 5. Case 1. a, Hemangioma of the skin of the neck and cheek. b, Appearance after a series of 12 treatments consisting of the injection of permanent pigments into the derma.

Fig. 6. Case 6. a, Capillary hemangioma of the cheek in a child 3½ years old. b, Appearance after one treatment consisting of intradermal injection of pigment. Avertin anesthesia was necessary. It was possible to cover the entire area in one treatment but complete obliteration of the color of the hemangioma was not effected. Further treatment is planned for this case.

Fig. 4.

Fig. 5.

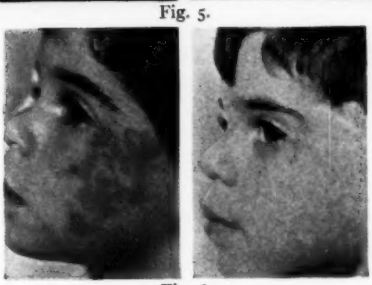

Fig. 6.

Neutralization of Color in Capillary Hemangiomas of the Face by Intradermal Injection (Tattooing) of Permanent Pigments.—Herbert Conway and John P. Docktor

(Legend on opposite page)

pigment of the skin in its upper layers thus giving the effect of dark red to purple. In order to overcome the abnormal color of the capillary hemangioma it is desirable to concentrate the pigment in the derma, deep to the stratum germinativum of the epidermis and superficial to the vascular dilatations of the capillary hemangioma. Since Figure 2 and microscopic sections from other tattooed capillary hemangiomas have shown the concentration of tattoo pigment to be in the upper layers of the derma, it is believed that any pigment which may have been deposited in the epidermis subsequently is lost through desquamation and that pigment which may have been injected into the capillary sinuses is carried off in the blood stream.

CASE REPORTS

Cases 1 to 7 are examples of port-wine stains or capillary hemangiomas. As described by Lister these are sharply defined areas of intense erythema, usually about the face and neck and not elevated above the surrounding skin. Present at birth, they do not extend to involve new areas of the skin and they show no tendency to spontaneous regression. Table I lists the size and location of lesions, the number of treatments, the combination of pigments and the results.

SUMMARY

Report is made of 7 cases in which intradermal injection of insoluble pigment through electromagnetic needles (tattooing) has been used in the neutralization of the color of capillary hemangiomas. The management of these cases required a total of 40 treatments. With one exception these treatments were done without anesthesia. The exception is the case of a 3½ year old child in which the single treatment was done under avertin anesthesia. There have been no complications. Microscopic sections of capillary hemangiomas so treated have shown that the desired result is obtained by injection of the pigments into the upper layers of the derma. All of the patients with capillary hemangiomas have been satisfied with the result of treatment. The technique of administration and a description of apparatus and pigments are given. Opinion is advanced that the intradermal injection of permanent pigments (tattooing) is a method of treatment which satisfactorily neutralizes the color due to capillary hemangiomas.

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PRESERVATION OF JAW FUNCTION FOLLOWING SURGERY AND TRAUMA

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OPERATIONS on or trauma to the jaws, the adjacent cheeks, or in the neighborhood of the joints may jeopardize function. The mandible, being the moving member, is the part usually causing the most concern.

Removal of a section of the mandible creates an immediate and serious problem in management of the remaining fragments (1). If not controlled and held in proper relationship, the attached muscles may pull the fragments medially and backward, allowing the tongue to fall back in the throat and shut off the airway (Fig. 17). When such a patient survives the initial breathing and feeding hazards, the secondary repair of the bony defect is needlessly complicated by the necessity of laboriously restoring the fragments to their original relationship before the bone graft can be done (Figs. 7, 12). This is particularly difficult when the posterior fragment has been pulled up into the temporal fossa and fixed there by shortened muscle and scar. An unnecessary oral fistula may further complicate the problem, prolong the rehabilitation, and make the patient miserable. Such operations often entail the loss of soft tissue with the formation of binding scar. Even resection of the part thickness of the mandible may produce this same result, if not this extreme, at least causing a loss of the buccal sulcus and inability to wear a denture.

Mandibular resection is usually performed as a planned procedure so that an adequate scheme is prepared in advance (1). Occasionally, however, one may be faced with the traumatic loss of bone creating the same problem. Where available, the simplest and best procedure is simply to wire the teeth of the fragments to their corresponding maxillary teeth (Fig. 12). Table IA indicates the mechanical possibilities where both fragments contain teeth. When partially or wholly edentulous, or in children, where the teeth are not adequately developed, the problem is more difficult and the schemes available without preliminary preparation are few. The appliances adapt-

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Fig. 1. Result following resection of the mandible for early osteogenic sarcoma. The mandible was resected and an internal bar inserted, the patient leaving the hospital entirely healed within 10 days. The bar is in place as shown 14 months after operation. There is no drainage and no evidence of bone reaction. Patient is allowed to chew soft foods. The mandible feels reasonably solid to palpation and there is only slight deviation of the chin on opening of the mouth. Eventually a bone graft will be required if the malignancy proves to be controlled.

Fig. 2. Result following upper neck dissection, resection of the mandible, and a large area of buccal mucosa for a carcinoma arising on the alveolus. Internal bar was inserted at operation as shown. Patient was healed within 3 weeks and returned to work within 6 weeks after operation. The bar is present without reaction or drainage 10 months after operation. Eventually the bar will probably be removed or supplemented with a bone graft.

able to this problem are outlined in Table I—B and C.

TABLE I.—APPLIANCES USED TO CONTROL FRAGMENTS OF MANDIBLE AFTER RESECTION

A

Appliances which utilize teeth (intraoral): posterior fragment contains teeth

a.* Interdental wires.
b.* Arch bars.
c.* Swaged metal splint (with or without jack-screw).
d. Splint on teeth with dependent part separating bone.

B

Appliances which utilize bone and teeth (intraoral and extraoral): short edentulous posterior fragment

a. Wire teeth in occlusion and use modeling compound in molar area to keep posterior fragment down.
b.* Arch bar or splint with posterior fork to keep posterior fragment down.
c.* Arch bar or splint on mandible with posterior portion accurately fitted to junction of body and anterior border of ramus. (Herpin splint with or without jack-screw.)
d.* As in (c) except arch bar or splint applied to maxilla with interdental wiring.
e. Arch bar or splint with posterior part attached:
   1. Directly to bone.
   2. To bone screw.
f. Wire passed through drill hole near angle of mandible and attached posteriorly to head cap and wire rest of jaw in occlusion.

C

Appliances which utilize bone (intraoral and extraoral): Number of teeth and size of posterior fragment not necessarily a consideration

a.† Bone screws (and bar) inserted with each fragment. (Stader, Berry, Griffin, etc.).
   1. Intraoral.
   2. Extraoral (preferred).
b. Kirschner wires (modified) passed through fragments.
c. Bar interposed between ends of fragments (Figs. 1, 2, 3, 4, 5, 6, 17).
d.* Open bite splint attached with circumferential wires.

*Also controls fragments adequately for insertion of bone graft.
†Not ideal for bone graft because of local osteomyelitis around bone screws and subsequent loss of stability of splint.

Because of the difficulties involved in repair following jaw resections, it is desired to call attention to the operation of subperiosteal resection (2). It has frequently been observed that the mandible will regenerate with surprising adequacy after the sequestration of large segments following osteomyelitis (Fig. 16). Similar regeneration will occur following subperiosteal resection (Figs. 3, 4, 5).

Obviously, this procedure cannot have widespread application. Subperiosteal resection is inadequate in the treatment of many tumors; it could rarely be safely performed in the treatment of any of the malignancies. Occasionally in dealing with adamantinomas, os-

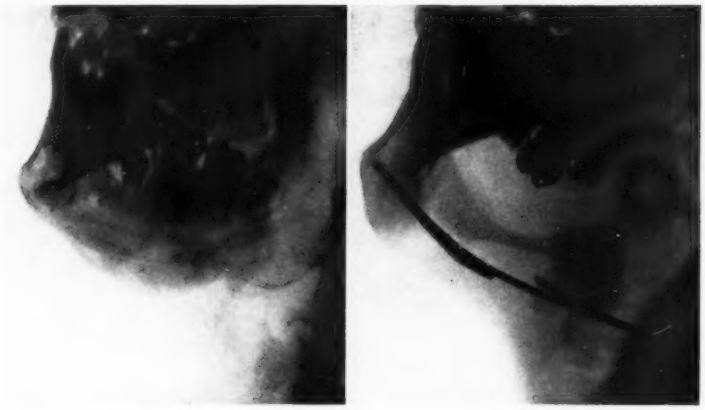
Fig. 3. a, Photograph of 8 year old child before operation showing enlargement of right jaw. b, Five months after subperiosteal resection of the mandible. Microscopic diagnosis of tumor removed was ossifying fibroma. (Plastic and Reconstructive Surg., 1946, 1: 238.)

a b c

Fig. 4. a, Preoperative roentgenograph of tumor. b, Immediate result of subperiosteal resection. c, X-ray film taken 8 weeks following subperiosteal resection and insertion of internal bar. A strand of lingual periosteum was preserved which supplied regeneration as shown in this short period of time. Wound has healed 10 days after operation. There has been no subsequent inflammation or drainage, and at the end of 26 months, the bar is still in place and the mandible strongly healed. (Plastic and Reconstructive Surg., 1946, 1: 238.)

sifying fibromas, osteomas, or even with more simple tumors which have caused extreme expansion of the bone, the entire thickness of the bone must be removed, but some strands of periosteum can be left bridging the gap between the ends. If the fragments are adequately controlled, regeneration will readily occur especially in children (Figs. 3, 4, 5).

In dealing with children, splinting or interdental fixation is unsatisfactory. The same may be true in adults if the fragments are wholly or partially edentulous. In such cases holes may be drilled in the ends of the bones and a bar of stainless steel inserted to bridge the defect (Figs. 1, 2, 3, 4, 5, 6, 17). Surprising rigidity results from this procedure and al-



a b

Fig. 5. a, Tumor of mandible in a 9 year old boy. At operation it was found that the entire thickness of the mandible was expanded and it seemed impossible to remove the tumor adequately and retain any bone at the tumor site. The periosteum was not involved except near the alveolus. A subperiosteal resection was performed and an internal bar inserted. The wound was completely healed in10 days. No interdental fixation was required. b, Regeneration present 7 weeks following operation. Repeated x-ray films have been made to date over 18 months' time. No evidence of bone reaction is present. Wound is healed. The bar is still in place and there is no external deformity. (Plastic and Reconstructive Surg., 1946, 1: 237.)

Fig. 6. Roentgenogram of mandible of an 83 year old man following operation for carcinoma of the buccal mucosa and alveolus with metastasis to the upper neck. Oral portion of dissection was done with the cautery. An internal bar was inserted as shown. The neck wound was packed open because of the cauterized wound which was present. This healed down to a very small oral fistula which was closed 4 months after the operation. Although there was no reaction around the bar, it was removed at that time, having served its purpose of maintaining normal position of the fragments during the period of soft tissue healing. Especially in older people it is important to maintain the rigidity of the mandible during the immediate postoperative period to minimize respiratory difficulties.

a b c d

Fig. 7. a, c, Front and profile photographs of a patient who had lost anterior portion of the mandible from bicuspid to bicuspid area and soft tissue of the lip, chin, and floor of the mouth as the result of a gunshot injury. Note the narrowness of the face over the region of the angle of the mandible, the result of the remaining portions of the mandible being pulled inward by scar. Two previous attempts at bone graft elsewhere had been unsuccessful because of the inadequacy of the soft tissue covering. b, d, Front and profile views of the same patient following restoration of soft tissue lining of lip and floor of mouth and covering of the chin and successful bone graft as shown in Figure 8. The lower lip was filled out by a triangular flap rotated from the center of the upper lip. Patient is wearing dentures.

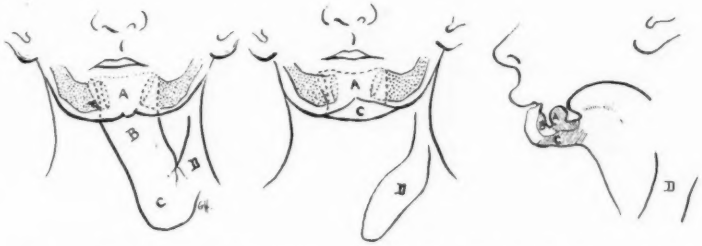


Fig. 8. Diagram illustrating source and use of the soft tissue flap for restoration of soft tissue loss in patient shown in Figure 7.

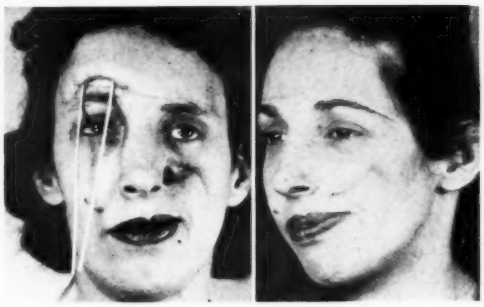
a b

Fig. 9. a, Huge ameloblastoma of the right mandible of 25 years' duration. b, Result following hemisection of mandible. There has been no bone restoration. The deviation of the remaining portion of the mandible from the midline is minimized by accurate closure of the wound, and maintenance of remaining fragment in normal position during the period of healing and subsequent scar tissue pull. (Surg. Gyn. Obst., 1945, 81: 577.)

though additional fixation is desirable for a time, if available, it is not essential. Where possible, the mucous membrane should be accurately closed to exclude the neck wound from mouth contamination.

Following the conventional resection of the mandible, the space retention apparatus must be worn long enough to insure that the fragments may be easily restored to their proper positions at the time for bone grafting. At such time some other scheme for fixation may be employed, possibly even utilizing the graft for partial fixation.

Soft tissue considerations: before a bone graft to the mandible is done, adequate soft tissue covering for the graft must be present (Fig. 7). At the time of injury or resection, all possible soft tissue must be preserved. This entails accurate closure of wounds and avoidance of continued infection with resultant wasting of tissues (Figs. 9, 14). If the quality or amount of soft tissue is inadequate to cover the graft easily and heal readily afterward, it must first be supplemented with a skin graft, pedicle flap, or by mobilization of local tissues (Figs. 7, 8).



a b

Fig. 10. a, Defect of face, palate and lining of cheek resulting from radical operation for carcinoma of the antrum. Patient has inability to open the mouth because of fixation of the coronoid process in operative scar. Applicator sticks are inserted in skin lined pocket underneath forehead flap which has been prepared for use in soft tissue repair. b, Final result obtained by restoration of half of the palate and buccal mucosa, letting in the flap through the hole in the cheek. Mouth opening was obtained by intraoral resection of the coronoid process. Another section of the same flap was used to fill the cheek defect after severance of the pedicle from the portion reconstructing the palate.

Because of the nature of the defect following resection of the mandible, the graft must be of the onlay type applied along the inferior and laterial borders of the mandible and overlying the bodies of the fragments. If it is desired to place the graft between the ends of the bones, anatomically replacing the resected segment, then a pedicle flap must be used intraorally between the ends of the bones to provide a good strong covering which will not be torn at the time of the dissection for the placement of the graft (Fig. 8).

a b c d

Fig. 11. a, Front and profile views of a man 35 years old who has had ankylosis of the left temporomandibular joint since childhood. b, Correction of asymmetry of the mandible with cartilage transplant to make the chin more prominent and alleviate flatness over right mandible. Mouth opening was gained by resection of left temporomandibular joint.

a b

Fig. 12. a, Immediate defect produced by gunshot wound. There is loss of the entire symphysis of the mandible. b, Result from immediate closure of soft tissue wounds and interdental fixation of remaining segments of the mandible. Note that the maintenance of the fragments has prevented the flattening over the angles of the jaw obvious in Figure 7. Had not this fixation been employed, scar tissue traction would have drawn the two segments of mandible inward, making subsequent repair much more difficult.

a b

Fig. 13. a, Retrusion of the mandible, possibly due to childhood infection. This did not bother the patient until she lost all of her teeth. It was impossible to provide a satisfactory denture because of the extreme overbite. b, Wearing satisfactory prosthesis following insertion of cartilage to build out the mandible and give bearing point for prosthesis and enlargement of lower labial sulcus with free skin graft.

MOUTH OPENING

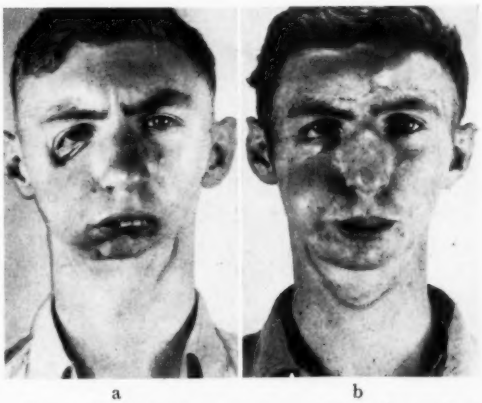
Inability to open the mouth following intraoral surgery may be the result of a number of things, singly or in combination. Trismus indicates a temporary inelasticity of the tissues joining the jaws, this inelasticity preventing opening. This is the result of inflammation, either active infection or that following recent manipulation.

Frequently, however, soft tissue inadequacy or scar freezing in areas of slight clearance may in itself cause a permanent false ankylosis (Fig. 10). Resection of the mandible, along with cheek mucosa, will not prevent the opening of the remaining large segment of the mandible because this is not directly involved in the tissue deficiency, but would not permit opening if a successful bone graft restored the mandibular continuity. Destruction of cheek lining, without its replacement, will bind the jaws (Figs. 9, 14). At the time of mandibular resection it is rarely feasible to replace cheek lining. Not infrequently, however, the excision of cheek lesions may immediately be followed by split thickness skin grafts to replace the desired surface area.

In dealing with such a scar tissue fixation, an accurate diagnosis of its extent is necessary. Simply cutting across such a contracting scar may give temporary relief but will be followed by healing to the original position. Removal

a b

Fig. 14. Result following disarticulation of nearly half of the mandible and removal of full thickness of portion of the left cheek for carcinoma of alveolar and buccal mucosa. Distortion of the remaining portion of the mandible has been minimized by maintaining it in normal position during the period of healing and scar tissue traction.



a b

Fig. 15. Underdevelopment of mandible as the result of osteomyelitis of facial bones in early childhood. The ectropion of the lower eyelid resulted from soft tissue and bony loss in the region of the orbital border. Mandibular correction consisted of (1) building forward the point of the mandible with two thicknesses of rib cartilage, (2) adding soft tissue to the chin by means of a pedicle flap, (3) creating a skin graft lined sulcus between the lip and the implanted cartilage, and (4) constructing a dental prosthesis to correct occlusion and give additional prominence to the lower lip and chin.

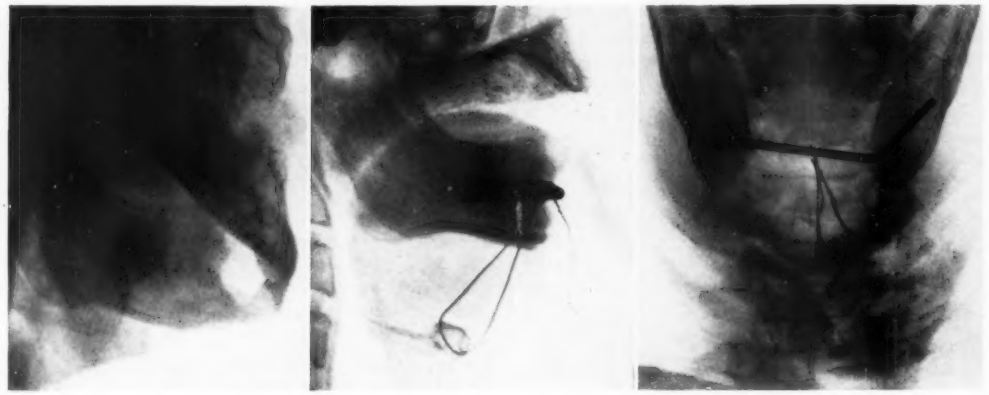
a b c

Fig. 16. a, Osteomyelitis of the mandible with pathological fracture. b, Beginning regeneration of mandible following spontaneous sequestration and control of infection by conservative means. c, Adequate regeneration of the mandible 4 months after acute infection. There is no external deformity. Radical surgery with removal of bone before spontaneous sequestration would surely have resulted in lack of continuity of the bone, necessitating bone graft.

of such a scar and covering the enlarged defect with a free skin graft if it is superficial, or a pedicle flap if deep, will give permanent relaxation (Fig. 10).

Subsurface scarring in the region of scant clearance between coronoid process and zygomatic arch may cause firm fixation in a closed position. This may result from operation, infection, or the use of radium in this neighborhood. Adequate resection of the coronoid to release one point of scar anchorage will give relief (Fig. 10).

Not infrequently mandibular resection with widespread soft tissue destruction is performed in cancer patients where restoration of mandibular continuity is not contemplated. Here it is desirable to maintain function as far as possible. Internal bar fixation, as described under subperiosteal resection, has been very valuable under these circumstances, inasmuch as the remaining fragments are retained in normal relationship, preventing immediate pharyngeal collapse with its dangers. Such fixation has been maintained without difficulty for several months, eventually working free. During this period, however, the open wound has healed without the contracture which would pull the remaining fragment well out of position, had not such fixation been maintained. Even though the patient's age and disease may not warrant complete repair, the disability has been minimized (Figs. 2, 6, 17).



a b c

Fig. 17. a, Roentgenograph of fibrosarcoma of the symphysis. b, and c, Roentgenogram showing resected area of the mandible with stainless steel internal bar fixation. The wire passes around the hyoid bone and holds the larynx forward to permit normal breathing. Resections of the symphysis region are especially hazardous unless some scheme is utilized to maintain the function of the genioglossus and geniohyoid muscle group.

Surgery, trauma, or infection in the neighborhood of the temporomandibular joints may result in either bony or fibrous ankylosis of these joints (Fig. 11). The intraoral use of radium or radon in this area may lead to such a condition. Frequently, in addition to the joint obliteration, the coronoid may be anchored to the zygoma (Fig. 10). In such conditions adequate resection of the joint, including the coronoid process, if necessary, will give relief. More dependence should be placed in the adequate removal of bone at the site of resection than in the application of some substance between the resected ends. If adequate bone is removed, the masseter muscle on the outside and pterygoid muscle on the inside will naturally fill the dead space between the cut ends, the amount of bone removed preventing reankylosing.

Under some circumstances this resection may be done from within the mouth. It is often more practical to make the approach from in front of the ear, reflecting the facial nerve downward, outward and forward, or from the neck, elevating all soft tissues, including the facial nerve, from the ramus of the mandible and beginning the resection on the ramus above the angle and working up to include the condyle and coronoid process. In some cases of ankylosis this is not too much bone to remove. Resection of the ramus of the mandible above the angle causes very little dysfunction and does not disturb dental occlusion, as does resection of the body.

To wear dentures successfully, the following factors must be considered: adequate mouth opening; mandible in continuity; adequate alveolar ridge and buccal sulcus to seat the denture; soft tissue of adequate quality, covering unavoidable irregularities; upper and lower arches of proportionate size (Figs. 13, 15).

The presence of other anchoring teeth may be of help in making up for some other deficiencies.

Following loss of soft tissue within the mouth or local removal of part thickness of the mandible, the prominence of the alveolar ridge may be lost. In such an instance, an adequate incision in the buccal sulcus and application of a split thickness skin graft may be adequate. One must plan for considerable shrinkage in such a graft.

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STUDIES IN THE ANATOMY AND REPAIR OF CLEFT PALATE

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WE did not have a clear understanding of the anatomy of the palate, and, particularly, of the physiology of the muscles associated with the palate, until we dissected the palate and structures associated with it. In fact, we did not comprehend the abnormal physiology of the cleft palate until we had dissected a cleft palate specimen and studied the deficiency in the bony anatomy of the palate in clefts. Apparently no one else understood it until the explanation of how velopharyngeal closure is produced was brought out in the literature. Wardill and Whillis, and Dorrance and Shirazy—all at about the same time—described how this function was performed. Hitherto, it had been thought that in cleft palates the soft palate was grasped in some way by the superior constrictor muscle, much the same as an obturator is grasped by the superior constrictor when a cleft exists.

Our anatomical studies show that closure is produced by the contraction of the superior constrictor muscle. Nowhere in the body that we know of is an orifice closed except by a complete circular muscle.

Material from American Oncologic Hospital and Doctors Hospital, Philadelphia.
Presented before the Clinical Congress of the American College of Surgeons, Cleveland, Ohio, December 16–20, 1940.

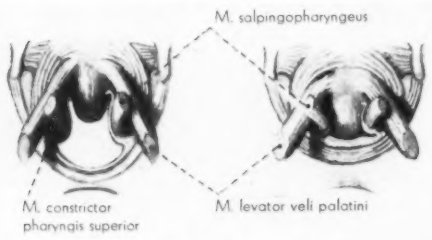

Fig. 1. a, left, Superior constrictor before contraction. Opening between nose and pharynx open. b, Superior constrictor in contraction. Opening between nose and pharynx closed.

The action of this so-called superior constrictor muscle is peculiar in that there is a compound action. If you will refer to Figure 1,a, you will get a more graphic conception of this muscle. The superior constrictor in the posterior pharynx is one muscle, having attachments on either side; as it comes forward, one part goes to attach to the hamular and pterygoid processes; the other splits off and is mesially attached to the soft palate, extending so far mesially that the fibers interlace with fibers of the opposite side. Figure 1, b, shows these muscles in contraction—that is, the superior constrictor has within its grasp the salpingopharyngeus muscle, as well as part of the levator palatini. This perhaps is better shown in Figure 2. Here you can note that the palate is fixed to the posterior nasal spine and posterior border of the bony palate. If this is so, then there can be practically no retroposition of the normal or cleft palate and its attachments during normal speech. If Figures 2 and 3 are studied it will be noted that when the fibers on the outer edge of the superior constrictor muscle which are attached to the hamular process contract, they draw the posterior wall of the pharynx forward. In this way, they put the inner portion or circular fibers of the superior constrictor in position so that, when they contract, they produce velopharyngeal closure. As previously stated, it is not possible to pull the palate backward because the superior constrictor muscles and the tensor palatine muscles are inserted into the palatine fascia, which, in turn, is inserted into the posterior border of the hard palate and to the posterior nasal spine. Now, after the repaired cleft soft palate has been displaced backward to its normal position, then this inner muscle, which is marked on Figure 2 as the palatine fibers of the superior constrictor, acts as a circular muscle and produces the closure. This is the

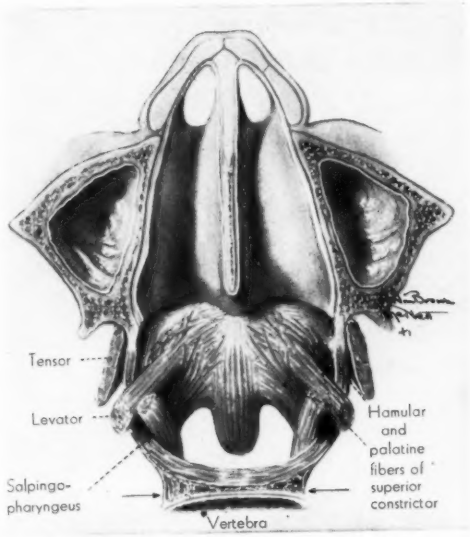

Fig. 2. Superior constrictor muscle at rest.

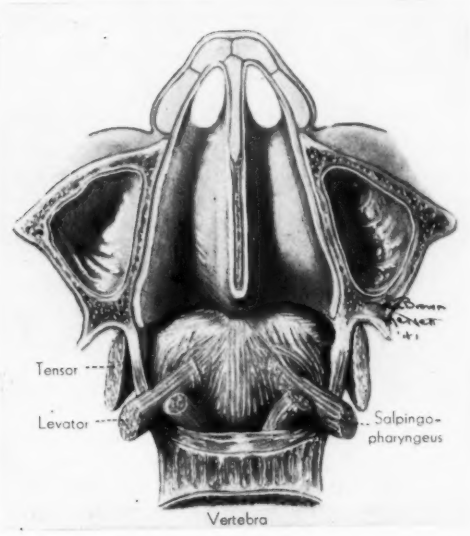

Fig. 3. Superior constrictor muscle in contraction.

Fig. 4. Normal bony palate showing posterior nasal spine.

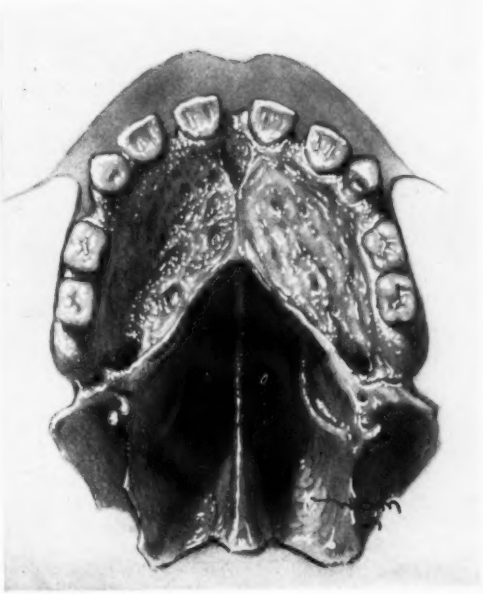

Fig. 5. Bony palate in cleft of the hard and part of the soft palate.

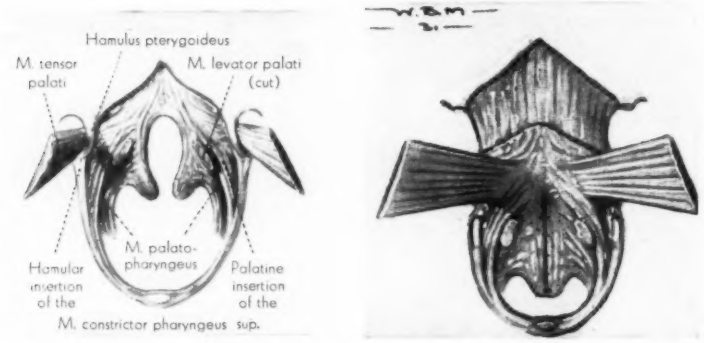

Fig. 6. a, left, Note size of opening before push-back. b, Note size of opening after push-back.

normal physiological action for closing off the nose from the pharynx.

To recapitulate: This physiological closure of the nose from the mouth was not understood by us until these studies were made. The normal closure is caused by the contraction of the outer fibers of the superior constrictor muscle which runs to the hamular process on either side pulling the posterior wall of the pharynx forward, thus permitting the inner portion of the superior constrictor muscle to act as a sphincter and produce closure. This anatomical physiological development was worked out by Dorrance and Shirazy (Figures 2 and 3).

If one knows the normal anatomy and then looks at a skull or, better, a dissection of a cleft palate case, as shown in Figures 4 and 5, one will note that in the normal palate there is a posterior nasal spine, and that the palatine

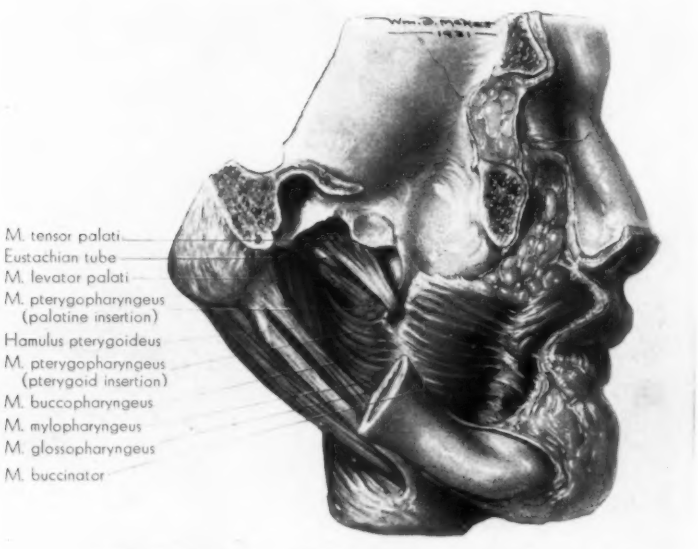

Fig. 7. Note size of the tensor palatine muscle.

aponeurosis is inserted into this area, as shown in Figure 4. In Figure 5, in which there is a partial loss of the hard palate, it will be noted that the palatine aponeurosis is inserted along the margin of the cleft palate, and, if Figure 6, a, is studied it will be noted that the space back of the palate is so great in diameter that the anterior ends of the inner portion of the superior constrictor can not close this opening because the palatine aponeurosis has been drawn too far forward into the cleft. This Figure 6 a and b illustrates a point that we particularly want to bring out. If the palate is retrodisplaced so that the portion of the palate which was normally attached to the spine is now put in the position where it would be if the spine were present, then the outer portion of the superior constrictor muscle can draw the posterior wall of the palate forward, thus allowing the circular portion of the superior constrictor to produce closure.

A study of Figure 4 shows the normal posterior nasal spine. Figure 5 shows the point at the apex of the defective bone. It can be easily understood how that portion of the aponeurosis which is normally attached to the spine is now pulled forward and attached along either border of the defect. In this position, if the two edges of the cleft were sutured together, there would be an extremely long space for the circular muscle to close, whereas, if you take the aponeurosis from each side of the bony cleft and retrodisplace it so that it would be where the normal spine should

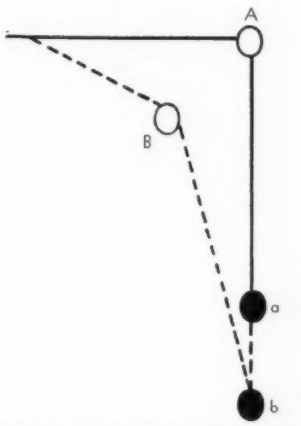

Fig. 8. a, Represents normal pull of tensor palatine muscle. b, After division of the hamular process, muscle becomes an elevator.

be, then you put the circular portion of the superior constrictor in a position to produce closure. This really is the physiology of the push-back operation.

It is well known that suturing together the two sides of a cleft palate, as in a Langenbeck operation, usually does not produce normal speech; yet if you take these patients and retrodisplace the palate so that the attachment of the palatine aponeurosis is displaced backward, the circular muscle portion of the superior constrictor is capable of obtaining velopharyngeal closure and normal speech ensues.

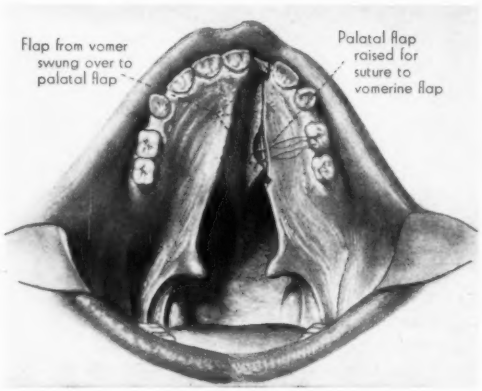

Fig. 9.

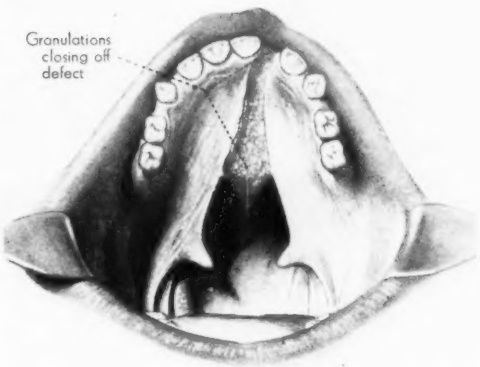

Fig. 10.

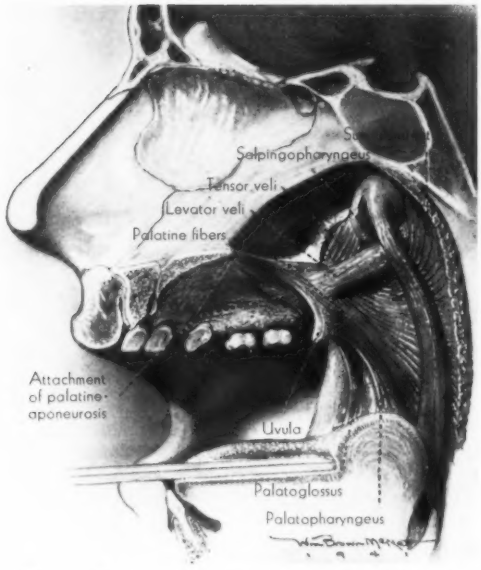

Fig. 11. Note pull of levator palati before push-back.

Recognition of the existence of this anatomical defect automatically excludes the use of the turn-over flap operations, such as those advocated by Lane.

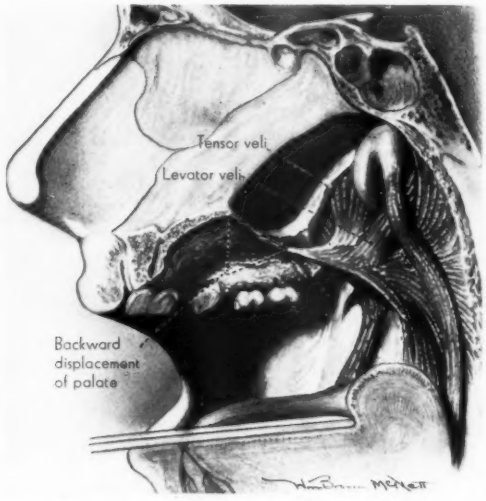

Fig. 12. Note pull of muscles after push-back.

In clubfoot, it is pretty well known that in certain cases there is a shortening of the tendons so that they must either be divided or lengthened before one can overcome the deformity. Well, a somewhat similar condition exists in the palate, where the tensor palatine muscle, due to the cleft, is shortened.

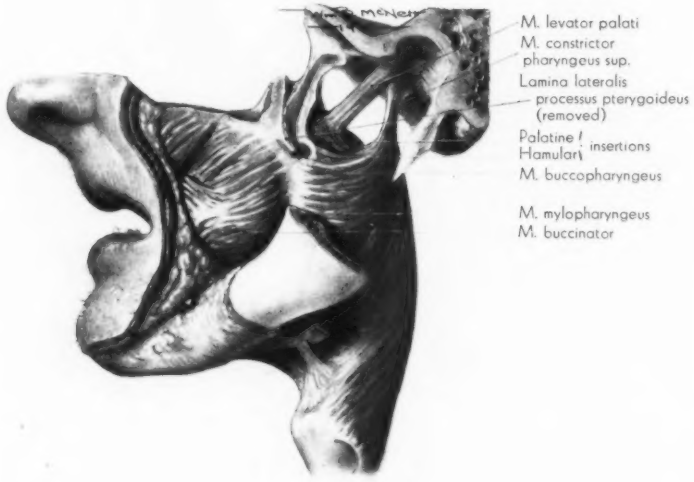

Fig. 13. Note insertions of palatine and hamular process.

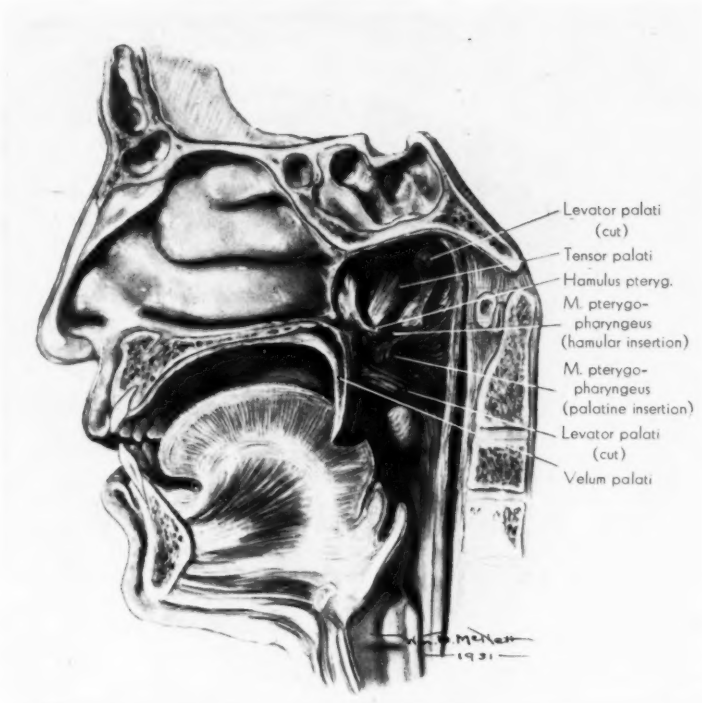

Fig. 14. Note two divisions of the superior constrictor, one going to the hamular; one going to the palate.

Surgeons wondered for many years why a hole developed in the middle of the palate following operations. If, for one moment, you would examine a cadaver and see this extremely large muscle, the tensor palatine (most of us are inclined to think of it as a little muscle), it would be easily understandable why such separation occurs, especially when there is a considerable pull (See Figure 7). For instance, when a child is under an anesthetic, these palatine muscles are stretched to get approximation of the palate; then, when the child comes out of the anesthetic, this shortened muscle which has been abnormally drawn over into the midline becomes active and, naturally, there is a pull on the suture line which may give way, and a hole results. In our push-back operations, we relieve this tension by dividing the hamular process, as recommended by Whitehead, or, if you prefer, by dividing the tensor palatine muscle, as recommended by Pollock. In this way you eliminate a big factor, causing the failure of the sutures to hold. This pull of the tensor palatine muscle was mentioned as early as 1846 by Liston. We have seen no harm from dividing the muscle, but think better of dividing the hamular process (Figure 8) which makes the tensor palatine muscle become an elevator instead of an abductor—that is, instead of being two sides of a right-angled triangle, it now becomes the hypotenuse.

These anatomical studies long ago proved to us that in cleft palate cases, each type is different. The main objective is to return the aponeurosis which is normally attached to the posterior nasal spine to its normal position; then closure is possible and normal speech becomes possible. As previously stated, the reason for defective cleft palate speech, after

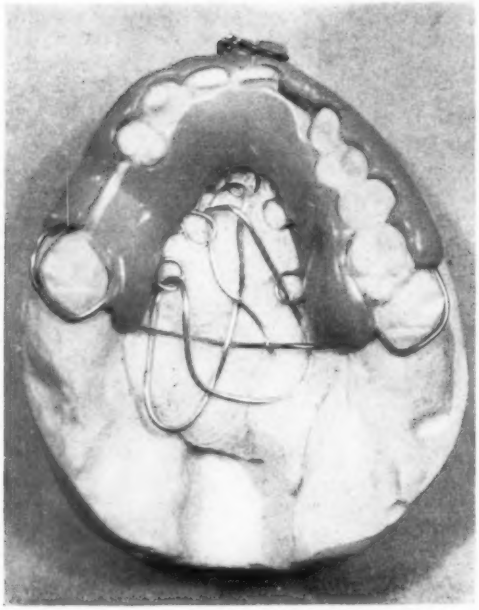

Fig. 15. Cleft palate splint with packing in place.

operation, is that the speech mechanism is defective; with this retroposition of the tissues to their normal position, we are now able to give the child a normal speech mechanism with which he may articulate properly. In other words, if you don't have a good speech mechanism, you can't expect good speech.

This in turn brings up a fact which we think should be strongly emphasized and which, after many years of experience in this type of surgery, we feel is correct. It is this: in the average case, you have only one chance to produce a perfect palate; therefore, extreme care and study should be given to the case. We have long since realized that early operations are not at all essential—in fact, failure in cleft palate repair in very young children is so common that now we do not advise operative work being done on a child until about the fourth or fifth year. We formerly had many partial failures and complete failures, whereas now that we are doing the operations later, we are having fewer failures. Nowhere else in surgery is the value of delayed flaps so essential, for if you lose a flap, you have difficulty in finding other material to take its place. We frequently raise flaps and suture them back, and then wait several weeks or months before completing the flap transfer. We are not unmindful of the advice given by others that the earlier these patients are operated upon, the better the speech will be. We know that this is not true and yet many surgeons say: "If only I had operated on the patient earlier, I then could have gotten a better result." This in our opinion is erroneous. Our feeling at present is that the most favorable time to operate is from the fourth to the sixth year. We find that the speech in our average case is better than when we operated earlier. In our experience, there are less anatomical failures, less loss of flaps, and speech is much superior to that which was obtained with the earlier operation.

In the past, the mortality rate of cleft palate operations was high. It still is higher than it should be. It can be definitely stated that the mortality rate is lower at the fourth year than at the first year, and the speech is better when the operation is delayed. We can see no justification for a hurry-up operation; the statement that the case should be operated on early and that, if it is not operated on before the time for the development of speech, the child will never develop normal speech, is not true—in fact, the reverse is nearer the truth.

We take it for granted that some form of push-back is essential in almost every palate case. We know that it is the only operation that is of value in cases of congenitally short palates; we know that in clefts of the soft palate it gives extremely satisfactory results. That leaves cases of complete clefts, unilateral or bilateral, to be considered. These, again, must be divided into those that have a vomer attached to one side of the cleft and those that do not have a well developed vomer. In those that have the vomer attached, we use our own vomer flap operation, as illustrated in Figures 9 and 10.

In our anatomical descriptions, we would like to show you Figures 11 and 12, which illustrate very definitely the change in insertion and pull of the palatine muscles,

before and after their retrodisplacement. We are now able by our push-back operation to obtain good speech for those cases which had been repaired by the von Langenbeck method, where velo-pharyngeal closure was not obtained. In these cases we are using a modified push-back in which we first raise the flap and cover the raw surface with a skin graft so as to produce a freely movable palate. We think the skin graft prevents scar and contracture.

Sometimes we have a hole remaining in the anterior part of the mouth. If this does occur, it gives us very little concern, as a plate will cover it without much difficulty (Figures 13 and 14).

Figure 13 illustrates by a photograph of the dissection how the superior constrictor muscle goes into the hamular process and its circular portion swings around the levator palatine. Figure 14 shows the superior constrictor, one portion going to the hamular process and the other portion going over to the palate. It also shows the large size of the tensor palatine muscle.

We would like to add that in all cleft palate operations, where teeth are present, we are now using a splint as a means of protecting the suture line. This is true in vomer surgery, as in any other surgery of the palate (see Figure 15).

GRADUATE TRAINING IN SURGERY

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DISCUSSIONS of graduate training in general surgery and the surgical specialties at the Clinical Congress at Cleveland centered chiefly in two aspects. One was the development of additional programs of residency training to meet the present extraordinary requirements. The other was the importance of the medical school in graduate training, particularly the methods of incorporating the basic medical sciences into training programs.

In tracing the progress made in the manner of treating the basic medical sciences since even the more recent prewar years, several important tendencies are evident. Among these are greater emphasis on the basic sciences, other than anatomy and pathology, which include biochemistry, physiology, bacteriology and pharmacology, and upon clinical rather than didactic teaching. The review courses have given way to the study of these more or less exact sciences as they bear directly on clinical procedures. The necessity of adequate knowledge of the applied basic medical sciences being established, the problem shifts to the hospitals in which the training programs are prepared and carried on. Frequently this calls for co-operation between the hospital and the medical school.

A panel discussion of graduate training in general surgery and the surgical specialties from the standpoint of the American College of Surgeons, the university-connected hospital, the hospital not connected with a university, the Veterans Administration hospitals and the graduate medical school, being open to hospital representatives as well as surgeons, developed free exchange of ideas by practically all agencies involved.

Representatives of the Department of Graduate Training in Surgery of the American College of Surgeons described the existing situation as to approved residencies and the work of the College in assisting hospitals possessing potentialities to develop graduate training programs and those hospitals now conducting residency programs of 2 years' duration to rearrange them to conform with present requirements as to content and duration. The interest of residents now receiving training of inadequate scope was emphasized. The benefits accruing to hospitals by modernizing their programs were described. They can by so doing maintain their status as modern teaching institutions and will be enabled to meet the situation when the wartime supply of residents will have become exhausted and hospitals may then be on the lookout for residents instead of the reverse order of today. Internes of the future will be looking for residencies which meet the requirements of accrediting agencies.

Having in mind the probability that more hospitals might be brought into the sphere of graduate training in surgery if assistance of medical schools were made available, a member of the staff of the Department of Graduate Training in Surgery has visited more than fifty medical schools throughout the United States and Canada. He developed interest in collaborative programs and discussed at each medical school particular problems. Surveys were made of hospitals offering the best opportunities for development of co-operative programs in order to ascertain the amount and character of assistance required by each. As a result of these efforts it has been possible in many places for the medical school to become the center of a collaborative regional effort.

At the present time thirty medical schools are offering varying types of assistance in co-operative graduate training. Others are preparing to do so. Such assistance will not only increase the number of approved programs but will tend to improve the quality of training in many programs which have already been approved by bringing the hospital permanently into the sphere of influence of the medical school.

The university-connected hospitals are situated more fortunately than any others in availing themselves of medical school re-

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sources. The methods of supplying this need which centers chiefly around the basic medical sciences have changed recently because of the added burden falling upon medical schools. Some schools formerly carried on this training by distributing its component parts to the undergraduate departments. Recently the tendency has been to develop a comprehensive "course" in the applied basic medical sciences and closely allied clinical training under central authority. By this means uniformity of training is insured and can be made available to larger numbers of trainees including those from affiliated hospitals. These courses have been lengthened from several months to as much as nine months because of this added requirement coming especially from returning medical veterans. Perhaps a more difficult problem is to supply the more or less limited or special needs of residents in hospitals capable of providing the other elements of the residency program. Chief among these is surgical anatomy. In such instances no procedures of universal application are possible. Recourse to the preclinical department of the medical school is often necessary but with the necessity of practical teaching ever in mind.

It is the consensus that the graduate medical school course, usually of eight or nine months' duration, provides the most satisfactory training in the applied basic medical sciences and allied principles of surgical technique as the basis for continued study and work connected with this important feature of surgery throughout the years of residency. Just when an academic year at a graduate school is most advisable has not been generally agreed upon. Graduate schools are furnishing some of their graduates to hospitals. Others are receiving residents who have completed part of their training, usually the first year.

Opening the field of graduate training to such smaller hospitals as are found capable of making a contribution of a supplementary nature to training programs centering in larger institutions will broaden the training and supply missing elements in programs, particularly in the surgical specialties. This is exemplified by some children's hospitals which can provide one year of training in children's orthopedic surgery needed to round out the program confined largely to adult orthopedic surgery and fractures in another hospital. This project had occupied the attention for several years of the Joint Committee of the American Orthopedic Association and the American Academy of Orthopedic Surgeons, and the American College of Surgeons has formally approved a number of such programs as well as others in pediatric surgery under similar circumstances.

The educational policies of the newly established Medical Department of the Veterans Administration emphasize a trend in medical education which will be of great importance in years to come. The basic feature is the close association of Veterans Hospitals with nearby medical schools whose faculties have been drawn upon to improve professional service and to supervise or conduct training programs substantially meeting the fundamental requirements of the American College of Surgeons. Today fifty-seven medical schools are working through their Deans' committees with fifty-two Veterans Hospitals. Consultants from the faculties of these schools and associate "attendings" have contributed to the establishment of a system of residency training that has won the admiration of the profession. About 1500 medical veterans are now receiving graduate training in these hospitals. This is relieving a serious situation confronting medical veterans in need of training at a time when civilian hospitals are overtaxed. The expected mass hospitalization of veterans may be utilized eventually in graduate training on a correspondingly large scale.

Virtually the same principles are being put into effect in the graduate educational procedures of the Army, Naval and Public Health services and as already noted these policies are spreading to all communities where such cooperation is found practicable. The improvement in the care of veterans and assurance of the continued association of highly trained consultants under an improved system of hospitalization means that there will be a continuation of the high esteem in which the public now holds the medical profession for the unprecedented service which it provided during World War II.

GENERAL REVIEW, 1946 CLINICAL CONGRESS

MALCOLM T. MacEACHERN, M.D., Chicago, Illinois

THE Clinical Congress in Cleveland was an event that adds another bright memory to the record of successful episodes in the history of the American College of Surgeons. Meeting rooms overflowed, interest ran high, and the education of the surgeon was advanced through the presentation of talks, clinics, demonstrations, and discussions covering developments that have occurred in the five years since the last Congress was held. Neither the time—the week before Christmas—nor the postponement from the September dates originally planned for the Congress in New York—were deterrents to the surgeons who wished to take advantage of the opportunities for learning about new ideas and techniques.

The Committee on Local Arrangements, of which Dr. Thomas E. Jones was Chairman, is to be highly commended for its help in arranging the excellent clinical program which was developed in the local hospitals, and for its many other activities in connection with the planning and conduct of the Clinical Congress.

The setting in the Cleveland Public Auditorium made the Congress quite different from preceding meetings, usually held in hotels. Arrangements for display of exhibits in the Arena were ideal, and meeting rooms were ample in number and, with a few exceptions, sufficiently large to accommodate the audiences. Two of the noteworthy exceptions were the symposia on Fractures and on Cancer, attendance at which overflowed the capacious fourth floor Ballroom. The experience demonstrated the desirability of again giving great emphasis to these two subjects in the 1947 Congress.

It is customary to select a dominant note about which to focus the impressions of any meeting. In connection with the Cleveland Congress, that is hard to do. There were many subjects concerning which interest was especially keen. Doubtless developments in the field of cancer attracted the most notice, although since cancer is a disease which attacks any part of the body, discussion of its treatment consequently comes up in meetings devoted to almost any specialty.

Since this special issue of SURGERY, GYNECOLOGY AND OBSTETRICS carries most of the papers which were presented at the more formal scientific sessions, it will be unnecessary here to mention their content. It would be very advantageous if in addition we could present summaries of the excellent panel discussions which were held, but this is not practical mainly because of lack of space.

The forums on Fundamental Surgical Problems have won an established place of great importance on the Clinical Congress program. It would be impossible to overestimate their value as an incentive to the younger surgeons and an avenue for the reporting of the results of the latest research. A few of the presentations are published in this issue.

The sessions of the Hospital Standardization Conference were interesting and stimulating. The meetings were successful in giving opportunities for helpful discussion of the many pressing problems that must be met in hospitals today. Nursing service naturally occupied a foremost place among the subjects listed, and solutions to the problem of shortages were presented in suggestions to improve personnel policies, to stimulate recruitment of student nurses, and to train a secondary group to assist the graduate nurse. The improvement of medical records, the education of the hospital trustee, the responsibility of the administrative staff in handling emergencies coming to the hospital and occurring within it, and the training of hospital personnel, were other subjects to which entire sessions were devoted.

A preliminary summary of the 1946 Hospital Standardization report was presented by Dr. Irvin Abell, Chairman of the Board of Regents, at the opening General Assembly. The report showed 3,118 hospitals approved—79.3 per cent of the 3,934 which were under survey during the year.

Associate Director and Chairman, Administrative Board, American College of Surgeons.

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HOSPITALS AND REPRESENTATIVES

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Cleveland Clinic	ROBERT S. DINSMORE	Mt. Sinai Hospital	RUDOLPH S. REICH
Evangelical Deaconess	OLIVER A. WEBER	Polyclinic Hospital	HENRY A. SCHLINK
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Grace Hospital	L. J. STERNICKI	St. John's Hospital	FARRELL T. GALLAGHER
Huron Road Hospital	HENRY W. BROWN	St. Luke's Hospital	DONALD M. GLOVER
Lakeside Hospital	FREDERICK R. MAUTZ	St. Vincent Charity	OLIVER A. WEBER
Lakewood Hospital	C. LEE GRABER	U. S. Marine Hospital	MARK E. MEYERS
Lutheran Hospital	FRANK S. GIBSON	U. S. Veterans Hospital	PHILIP F. PARTINGTON
	Woman's Hospital	ERNEST COX	

THE CLINICAL CONGRESS TECHNICAL EXHIBITION

LEADING manufacturers of and dealers in surgical instruments, hospital apparatus and supplies, diagnostic and therapeutic apparatus, pharmaceuticals, and publishers of medical and surgical books represented in the Technical Exhibition at the Cleveland Public Auditorium, Cleveland, Ohio, December 16–20, 1946:

Acme Engineering Co., Inc., Greensboro, N.C.
A. S. Aloe Co., St. Louis
American Cystoscope Makers, Inc., New York
American Hospital Supply Corp., Evanston
American Sterilizer Co., Chicago
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Liebel-Flarsheim Co., Cincinnati
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Medical Bureau, Chicago
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Merck and Co., Inc., Rahway, N.J.
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Picker X-Ray Corp., New York
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Rexair, Inc., Detroit
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